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ABSTRACT

This dictionary attempts to define routinely used specialized language in the various areas of biotechnology, and remain suitable for use by scientists involved in unrelated disciplines. Viewing biotechnology as the practical application of biological systems to the manufacturing and service industries, and to the management of the environment, terms defined have been selected from as broad a spectrum as possible to include work accomplished by the following disciplines: (1) microbiology; (2) pharmacology; (3) biochemistry; (4) chemistry; (5) physiology; (6) chemical engineering; (7) genetic engineering; (8) enzymology; and (9) cell biology. The typical biotechnologist can utilize this dictionary to integrate specialized work with studies being carried out by collaborators in related fields, particularly with respect to differences in terminology, i.e., jargon. (JJK)

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THE LANGUAGE OF Biotechnology

A DICTIONARY OF TERMS

John M. Walker and
Michael Cox

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The Language of Biotechnology

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A Dictionary of Terms

John M. Walker and Michael Cox

Allan Whitaker, *Contributor*

ACS Professional Reference Book

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About the Authors

JOHN M. WALKER has been a Reader in Protein Chemistry in the Division of Biological Sciences, Hatfield Polytechnic, Hatfield, Herts, England, since 1980. Before that he was a postdoctoral research scientist at the Institute of Cancer Research, London, for eight years. Walker received a 1st Class Honors Degree in Chemistry and a Ph.D. in Biological Chemistry from University College, London.

For many years he was involved in studies on nonhistone chromosomal proteins. At Hatfield Polytechnic he has been increasingly interested in algal biotechnology (particularly the use of algae as a source of novel pharmaceutical compounds) and in studies of the factors responsible for protein stability (using protein engineering methodology).

Walker is coordinator of the Hatfield Polytechnic Biotechnology Unit. Since 1981 he has been the organizer of highly successful Introductory Workshops in Techniques in Molecular Biology. These workshops are held annually at Hatfield, and are also run in Yugoslavia, Norway, Pakistan, and India. He is coorganizer of Molecular Biology and Biotechnology, a one-week Royal Society of Chemistry residential school held at Hatfield every two years. In addition, he has served as editor of a number of books on molecular biology methodology.

MICHAEL COX is a Reader in Applied Chemistry at Hatfield Polytechnic, Hatfield, Herts, England, and lectures in the fields of inorganic chemistry, chemical technology, and biotechnology. In 1987 he was granted the title of Professor in recognition of his research activities. He received M.Sc. and Ph.D. degrees from University College, London.

Following a sabbatical at Warren Spring Laboratory, Department of Industry, Cox became interested in liquid–liquid extraction and ion exchange recovery of metals from waste feeds, a topic in which he is still actively engaged. This led to a general interest in downstream processing of process streams, including those derived from fermentation.

Cox is the author of many research papers and review articles. For many years he served on the Committee of the Solvent Extraction and Ion Exchange Group of the Society of Chemical Industry, completing a term as Chairman in 1988.

Preface

To define the term "biotechnology" or to describe the role of a biotechnologist is never easy. Such broad terms often mean different things to different people. As a starting point, let us define biotechnology as the practical application of biological systems to the manufacturing and service industries and to the management of the environment.

Yet such a brief description ignores the wide spectrum of related disciplines that must come together to commercialize a biological process. At one end of the spectrum, biotechnology involves work at the laboratory bench level, often aimed at identifying or constructing microorganisms or cells capable of providing products of economic value. This aim can be achieved by the molecular biologist who applies new methodologies that arise from developments in the biological sciences, especially in genetic engineering, to microorganisms, plant cells, or animal cells. Alternatively, microbial screening programs (which can involve a multidisciplinary team of microbiologists, pharmacologists, biochemists, and chemists) can result in the identification of microorganisms producing potentially useful metabolites.

Once the organism or cell of interest is obtained, it is necessary to develop the growth of the microorganism, animal cell, or plant cell on a large scale in an economically viable process. However, in plant biotechnology, growth of appropriately modified cells to give a plant with novel characteristics can sometimes be the ultimate goal.

Scale-up involves both the microbiologist's knowledge of microbial physiology–biochemistry and fermentation technology and the biochemical or chemical engineer's knowledge of reactor design, heat and mass transfer, and process control. Recovery of the desired product takes us into the area of downstream processing, which requires expertise in areas such as chemistry, biochemistry, and chemical engineering to develop the various large-scale methodologies for

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concentrating, extracting, and purifying the required product as economically as possible.

The diverse applications of biotechnological processes range from waste treatment and odor control to the production of reagents for the diagnosis and treatment of disease. Enzymes, for example, are used in a variety of processes, including enzyme reactors, washing powders, biosensors, and diagnostic kits. The use of genetic engineering, via site-directed mutagenesis, to design more stable enzymes for use in these biotechnological processes takes us back to the beginning of our biotechnology spectrum.

The typical biotechnologist will probably be an expert in one of these areas, but will need to integrate specialized work with studies being carried out by collaborators in related fields. Each worker will have to understand the language (the "jargon") of all the collaborators if their individual areas of research are to be integrated successfully.

In this dictionary we have therefore attempted to define routinely used specialized language in the various areas of biotechnology. Involved scientists should be able to read and appreciate texts relating to a particular area of biotechnology, even when this area is unrelated to their own disciplines. We will no doubt be accused of the sin of omission in our choice of terms to include in this dictionary. Because of the diverse nature of biotechnology, it is often difficult to know where to draw the line. Given the size constraints inherent in any book, this had to be a matter of personal choice. We thank Allan Whitaker for his role as contributor in producing this book, as well as Stephen Boffey (Hatfield Polytechnic), John Melling (Warren Spring Laboratory), and Michael Verrall (Beecham Pharmaceuticals) for their useful comments and advice.

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Abomasum: The fourth stomach of the calf. The source of rennet, the commercial enzyme preparation used in cheese making.

Abrasion: The treatment of barley during the malting process, resulting in mild damage to the husk and underlying layers. This treatment is carried out prior to spraying with, or steeping in, gibberellic acid. It allows the gibberellic acid to pass directly to the aleurone layer and thus uniformly accelerates the malting process.

Abscisic acid (ABA): An endogenous substance (hormone) that inhibits plant growth. ABA, which is normally associated with phenomena such as fruit drop, leaf senescence, and bud and seed dormancy, has found use in plant tissue culture media to reduce growth rates, thus increasing subculture intervals. Growth limitation, induced by hormonal inhibitors at low temperatures and under oxygen limitation, is a reliable and cost-effective way to maintain stable germplasm.

Absolute filter: A filter used for the removal of microorganisms from an air stream; the filter pore sizes are smaller than the particles to be removed (*compare with* Air filter). The steam-sterilizable cartridge filter may be of polytetrafluoroethylene or a similar material, with a uniform pore size of 0.2 μm. Pressure drops are greater than with an ordinary air filter.

Absorbance: A measure of the extent to which a beam of radiation, normally ultraviolet, visible, or infrared, is attenuated by transmission through an absorbing medium, which can be a solid, liquid or solution, or a gas. The absorbance (A) is defined as:

$$A = \log I_o/I$$

where I_o is the intensity of the incident radiation and I is the intensity of the transmitted radiation. Absorbance has now largely replaced the earlier term, "optical density." The variation of absorbance with concentration of an absorbing species often follows the Beer–Lambert law. This allows for determination of the concentration of an unknown solution. *See also* Absorption coefficient.

Absorbent: A material that can be used to absorb another substance.

Absorptiometer: An optical instrument that measures the attenuation of visible radiation passing through a liquid sample. It can be used to measure turbidity as the incident radiation is scattered by the suspended particles. Thus, the amount of attenuation can be related to the concentration of suspended solids. It is an instrument commonly used to monitor waste-treatment processes.

Absorption coefficient: The proportionality coefficient (k) of the Beer–Lambert law, the units of which depend on the units of path length (l) and solution concentration (c) employed. Thus

$$k = \frac{A}{cl}$$

where A is absorbance and k is the absorption coefficient. When c is in moles per cubic meter and l is in meters, k becomes the molar absorption coefficient ϵ, with the units of square meters per mole (SI System). It is very important to specify units when quoting absorption coefficients, because misleading information can be implied with regard to the relative intensity of spectral bands.

Absorption spectrum: A measure of the variation of absorbance with wavelength, frequency, or energy used to characterize the atoms or molecules.

Acceleration phase: The period of gradually increasing growth prior to the log phase in a microbial culture. After the introduction of a microorganism into a nutrient medium, there is an initial lag phase

of no growth. This phase is followed by the acceleration phase, an interval during which cell growth rate gradually increases until the cells reach a constant maximum rate. At this point the cells are said to be in log phase.

Acesulfames: A class of sweeteners used in the food industry, derived from oxathiazinone. Acesulfame-K, the potassium salt of the 6-methyl derivative, is about 130 times as sweet as sucrose.

Acetic acid (ethanoic acid): CH_3COOH. Industrially the most important of the organic acids, used in the manufacture of a range of chemical products (plastics, insecticides, etc.). It was originally produced by the microbial oxidation of ethanol, but this approach is not economically viable at present (except for vinegar manufacture).

***Acetobacter* sp.**: Gram-negative ellipsoidal or rod-shaped bacteria that oxidize a variety of compounds to organic acids (e.g., acetic acid). Abundant in fermenting plant materials and important in vinegar manufacture.

Acetogenic bacteria: Bacteria capable of reducing carbon dioxide to acetic acid or converting sugars quantitatively into acetate.

Acetone–butanol fermentation: The production of a mixture of acetone and butanol by anaerobic fermentation of glucose by *Clostridium acetobutylicum*. However, few industrial plants still produce these solvents microbiologically. Most acetone and butanol is currently produced by synthetic processes that use petrochemical raw materials.

Acetyl coenzyme A (acetyl CoA): *See* Coenzyme A.

Acetyl reduction assay: A method for directly measuring nitrogen fixation activity in plants. The reduction of acetylene to ethylene by the enzyme nitrogenase is determined by gas chromatography with a flame-ionization detector.

Acid proteases: Protein-hydrolyzing enzymes, which have maximum activity at low pH (normally in the pH range 2.0–6.0). The most extensively studied acid protease is pepsin, obtained from the stomach, although commercially used acid proteases are prepared from fungal sources. Acid proteases from *Mucor pusillus* and *Mucor miehei* are used as rennet substitutes in milk coagulation. *M. pusillus* is grown on semisolid medium, whereas *M. miehei* is grown in submerged culture. Acid protease is also produced commercially by the growth

of *Aspergillus oryzae* on semisolid media. It is used in the hydrolysis of soybean protein in soy sauce manufacture, for improving the baking properties of flour, and as a digestive aid.

Acidulants: Chemicals added to food as flavoring agents to impart a "sharp" taste to the food. The most commonly used is citric acid, produced by the fermentation of molasses or glucose hydrolysate by *Aspergillus niger*. However, malic, fumaric, and itaconic acids are also used.

Acoustic conditioning: A technique used to increase the size of suspended particles by the aggregation of small particles as a result of the application of low-frequency (50–60 Hz) vibrations. The technique is used in broth conditioning to improve the filterability of the system.

Acrylamide: *See* Polyacrylamide gels.

Acrylamide gels: *See* Polyacrylamide gels.

Actinomycetes: Gram-positive mycelial or rod-shaped bacteria with a tendency to branch. Some form spores in small groups, in chains of indefinite numbers, or in sporangia. The order includes the genera *Streptomyces, Micromonospora, Nocardia, Actinoplanes,* and *Streptosporangium*. Many species produce antibiotics.

Activated carbon: A form of finely divided carbon capable of absorbing substances. The carbon is sometimes specified by its source (e.g., coconut, bone) and is produced by high-temperature treatment in the presence of steam, air, or carbon monoxide. It can be used for decoloring solutions and for the removal of organic compounds from potable waters by its incorporation in percolating filters.

Activated sludge process: A process used in sewage and wastewater treatment whereby actively growing aerobic microorganisms are contacted with the effluent in the presence of dissolved oxygen. New biomass is ideally produced at a rate commensurate with the loss of solids from the effluent. This ideal is not always the case, because it depends on the mode of operation of the plant. It can be either a batch or a continuous system that is open to the air and agitated to increase air entrapment, thus optimizing the oxidative breakdown of organic matter. A certain degree of recycling is necessary to increase the contact time between the settled solids from the effluent, the active biomass, and dissolved oxygen. A number of basic designs exist, but they all have the same common aim of maximizing aeration.

See, for example, Deep-shaft airlift fermentor. Commonly used in municipal sewage-treatment plants.

Active transport: The movement of a solute across a biological membrane against its concentration gradient so that the concentration on the product side is greater than on the feed side. This process requires the expenditure of some form of energy, as it is not capable of proceeding spontaneously.

Activity: **Of an enzyme**: The amount of enzyme present in a particular preparation is usually expressed in terms of units of activity based on the rate of the reaction the enzyme catalyzes. The international unit of activity, U, is defined as the amount of enzyme that will convert 1 μmol of substrate to product in 1 min under defined conditions (usually 25 °C and the optimum pH).

: **Of immobilized enzymes**: *See* Effectiveness factor.

: **(Thermodynamic)**: A thermodynamic parameter that measures the "active" concentration (*a*) of a substance in a given chemical system, in contrast to the molecular concentration (*c*). These two terms are related by the activity coefficient (*f*) such that:

$$a = fc$$

f, a dimensionless parameter with a wide range of positive values, approaches unity in dilute solutions. However, in concentrated solutions *f* may become very large, thus increasing the "active" concentration over the molecular concentration. Activity is the parameter measured by electrochemical sensors such as selective ion electrodes. *See also* Distribution constant, Partition constant.

Activity coefficient: *See* Activity.

Activity yield (immobilized enzymes): *See* Effectiveness factor.

Adaptors: Short synthetic oligonucleotides with one blunt end and one sticky end. The blunt ends are ligated to the blunt ends of a DNA fragment, and thus produce a DNA fragment with sticky ends. This fragment can be joined to an appropriately cleaved vector by base pairing of sticky ends, followed by ligation.

Adjuvants: Substances added to antigens in order to intensify the immune response to the antigen when the mixture is injected into

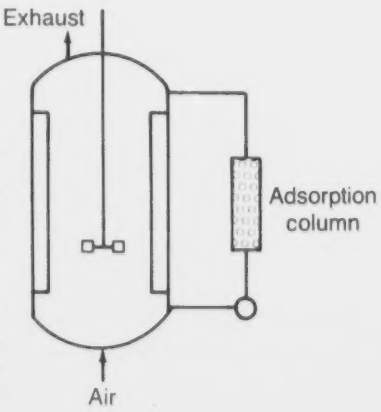
an animal. The most commonly used is Freund's complete adjuvant, which is a mixture of a white mineral oil (e.g., liquid paraffin), an emulsifier such as mannide monooleate, and heat-killed *Mycobacterium tuberculosis*. Freund's incomplete adjuvant lacks the tubercle bacilli.

Adsorption: In microbiology: The process whereby bacteriophages attach to specific receptors on the host cell prior to infection by injection of their nucleic acid.

: **In chromatography**: A term used to describe the binding of a ligate to the surface of an affinity adsorbant.

: **In surface chemistry**: A term used to describe the accumulation of molecules at the surface of a liquid or solid. This accumulation occurs as a result of the atoms at the surface having different properties from those in the bulk phase. The excess free energy of these surface atoms tends to attract foreign atoms or molecules. When they attach to the surface, these atoms lower the free energy of the surface. The adsorption process may involve either chemical or physical forces. *See also* Chemisorption.

Adsorption fermentation: A process by which products are removed from the culture broth by adsorption onto polymers, carbon, etc. Two configurations have been employed, suspension of the adsorbent in the fermentor and circulation of a stream from the fermentor through an adsorbent bed. The latter is generally preferred, as adsorbents may be toxic to microorganisms. A modification of the system uses ion-exchange resins to remove charged products. Also called extractive fermentation.



Adsorption isotherm: An equation that represents the adsorption of a substance onto a surface, which may be a solid or liquid, at constant temperature. Various isotherms have been devised to represent different forms of adsorption (e.g., Langmuir, Freundlich, and BET). The

adsorption isotherm is a factor in determining the shape of the breakthrough profile of an adsorption column. *See also* BET isotherm, Langmuir adsorption isotherm, Freundlich isotherm, Breakthrough profile.

Adventitious: An adjective used to describe organs developing from positions on a plant from which they would not normally be derived; for example, shoots from roots.

Aeration: The introduction of air or oxygen into a liquid, fermentor, or activated sludge plant. *See also* Sparger.

Aeration number (N_a): A term used in aeration–agitation studies in fermentors to relate gas-flow rates to impeller speed and diameter.

$$N_a = \frac{G}{ND_i^3}$$

where G is the gas-flow rate ($m^3 s^{-1}$), N is the impeller speed (s^{-1}), and D_i is the impeller diameter (m). It is used to relate power consumption in gassed and ungassed liquids

$$\frac{P_g}{P} = f(N_a)$$

where P and P_g are the ungassed and gassed power consumptions, and f is a proportionality constant.

Aerobe: An organism that requires the presence of molecular oxygen for growth.

Aerobic reactor: A reactor that is operated under aerobic conditions, with air normally used as the source of dissolved oxygen.

Aerobic waste treatment: The degradation of waste material by the use of aerobic microorganisms. A number of different designs of waste-treatment plants exist. *See* Activated sludge process, Oxidation pond, Deep-shaft airlift fermentor, Percolating filter.

Aerosol: A dispersion of finely divided particles of solid or liquid in a gas. The particles are often of colloidal size, as in smoke.

A-Factor: A bioregulator (3*S*-isocapryloyl-4*S*-hydroxymethyl-γ-butyrolactone) produced by *Streptomyces griseus* and other *Strepto-*

myces spp. Administration of very low concentrations of this compound will induce morphological differentiation and streptomycin production in certain mutant strains lacking the A-factor.

Affinity adsorbent: A support matrix coated with an affinity ligand that is capable of selectively adsorbing substances such as proteins, enzymes, and antibodies. *See* Affinity chromatography.

Affinity chromatography: A chromatographic technique that depends on the specific interaction of one molecule with another. It operates by the covalent attachment to an insoluble inert support of a specific ligand. The ligand must have a special and unique affinity for the molecule (ligate) to be purified. Because of this specific interaction the technique is capable of extreme selectivity, but it is also likely to be expensive. An example of the process is the separation of an enzyme by binding an analogue of its substrate to an inert matrix, thereby providing an opportunity for the enzyme to be retained on the support. A crude sample containing the enzyme (ligate) is run through the column under conditions that encourage binding of enzyme to ligand. Unretarded contaminants pass through the matrix and are completely removed by washing. The enzyme is then eluted by changing the environment to favor desorption (e.g., change in ionic strength of the buffer, change in pH of the buffer, or addition of a compound that competes for the binding to the ligand). *See also* Dye–ligand chromatography.

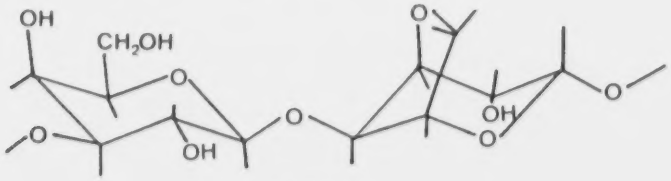
Affinity partitioning: A liquid–liquid separation process in which one phase has been chemically modified to include a ligand that has a specific affinity for the molecule to be separated. Thus, this compound tends to be concentrated in one phase to the exclusion of others in the feed mixture. After separation of the two liquid phases, the separated molecule may be released from the affinity ligand by alteration of the solution conditions, thus breaking any chemical interaction between the ligand and the desired molecule. *See also* Two-phase aqueous partitioning.

Agar: Also called agar–agar. A polysaccharide mixture isolated from certain agar-bearing red algae, especially *Gelidium* and *Gracilaria* spp. Agar comprises two fractions: a highly charged agaropectin fraction and a neutral agarose fraction. When agar is heated in aqueous solution and cooled, a gel is formed. If appropriate nutrients are included in this solution, the set gel forms an appropriate surface upon

which to grow microorganisms. When the gel is set in a Petri dish, this provides the "agar plate" much used by microbiologists. Because of the charged nature of agar, it is of little use as a support for electrophoresis or immunodiffusion. Agarose, purified from agar, is used for this purpose. Agar has also been used for the immobilization of cells in the form of spherical beads, blocks, or membranes. In the food industry it is used in soups, jellies, ice cream, and meat and fish pastes. It is not digestible by human beings.

Agaricus bisporus: The common edible mushroom. Commercial cultivation of this mushroom accounts for about 75% of the mushrooms produced worldwide.

Agarose: A purified linear galactan made up of the basic repeating unit agarobiose. It is purified from agar and agar-containing seaweed. When it is heated in aqueous solution and cooled, a gel is formed that is ideal as an inert support for electrophoresis, immunoelectrophoresis, and immunodiffusion. The gelling properties are attributed to both inter- and intramolecular hydrogen bonding. Agarose, a more porous medium than acrylamide, is usually used at concentrations around l%. Substitution of the alternating sugar residues with carboxyl, methoxyl, pyruvate, and especially sulfate occurs to varying degrees. This substitution can result in electroendosmosis during electrophoresis and ionic interactions between the gel and sample in all uses, both unwanted effects. Agarose is therefore sold in different purity grades, based on the sulfate concentration; the lower the sulfate content, the higher the purity.



Agarose

Agglutination: The formation of clumps of cells or microorganisms by linking cell-surface antigens with antibodies. Agglutination reactions are commonly used to identify blood groups, bacteria, etc.

Aggregation: The formation of large assemblies of cells, molecules, or particles. With particles, the process consists of two steps, flocculation and coagulation.

Agitator (impeller): A device to introduce turbulence in a mixture by shaking or stirring. Different commercially available agitator–impeller designs include flat blade, marine screw, turbine, and variable pitch screw. Selection of the appropriate device depends on a number of factors, including processing requirements, flow properties of the fluids, and materials of construction. The final choice often involves experience of performance with related systems.

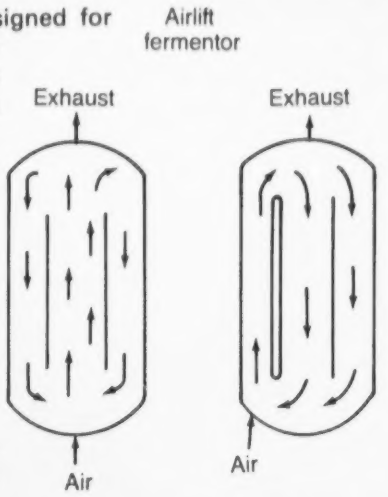
Agrobacterium tumefaciens: A Gram-negative soil microorganism that causes crown gall disease (transformation of plant cells to proliferating tumor cells at the crown, the junction of the root and stem) in many species of dicotyledonous plants. Crown gall disease is caused by the Ti plasmid (tumor-inducing) within the bacterium. After infection, part of the 200 kbp plasmid, called the T-DNA (15–30 kbp), is integrated into the plant chromosome and maintained in a stable form in daughter cells. The T-DNA genes expressed in the plant cells are responsible for the malignant transformation of the plant cells. Transformation of plant cells with *A. tumefaciens* containing engineered Ti plasmid vectors (e.g., "disarmed" plasmids that have had some or all of the T-DNA genes deleted, thus eliminating cancerous growth of cells) has potential for plant genetic engineering. However, at present the method is almost entirely limited to the transformation of dicotyledonous plants, whereas most important crops (e.g., barley, wheat, rice) are monocotyledonous.

Agrochemicals: Chemicals used for crop protection. They include pesticides, herbicides, and fungicides.

Agronomy: The branch of agriculture dealing with crop production and soil management.

Air filter: A filter used for the removal of microorganisms from an air stream connected to a fermentor, a clean room, or a sterile cabinet. The pore sizes in the filter are larger than the diameter of the particles to be removed (*compare with* Absolute filter), and therefore this system relies on the depth of the filter bed to completely remove particles by adsorption onto the fibrous structure. The filter bed is made of a fibrous material such as cotton, glass, slag, or steel wool. The gaps between the fibers are normally in the range 0.5–15 μm. Fibrous filters are preferred to absolute filters in the fermentation industry because they are more robust, cheaper, and produce lower pressure drops. The filters may be steam-sterilized before use. *See also* Absolute filter.

Airlift fermentors: Bioreactors designed for aerobic fermentation where agitation is provided solely by the sparge air. Three basic designs exist. In the concentric draft tube (internal loop) design, the bioreactor contains a concentric draft tube and air is sparged into the base of the draft tube; this causes media circulation as shown in Figure a. Alternatively, air can be introduced at the base of the annulus between the draft tube and column wall to regulate the direction of circulation, as shown in Figure b. The tubular loop (external loop) fermentor consists of two columns in parallel, connected top and bottom. A number of variations of these basic designs exist. Because shear forces are small, this method is ideal for the growth of animal and plant cells, which are very fragile. *See* Deep-shaft airlift fermentor, Gas lift.



Alfa Laval contactor: A centrifugal device for liquid–liquid extraction, consisting of a vertically mounted bowl rotating about a central shaft. The bowl consists of concentric channels with spirally wound baffles to control the flow paths of the two fluids. The baffles also provide regions of intense mixing as the heavier fluid moves toward the bowl periphery and the lighter fluid moves toward the bowl axis. *See also* Podbielniak extractor.

Algae: A large group of unicellular and multicellular eukaryotic aquatic plants, normally photosynthetic and pigmented. Some classification systems also include the prokaryotic cyanophyta under the name blue-green algae, although ideally they are bacteria or cyanobacteria. Algae exist in both freshwater and marine environments. They are used commercially for the production of a range of compounds including agar, agarose, alginate, and carrageenan. They are also used as a source of pigments (e.g., β-carotene) and have been used to provide single-cell protein, particularly in tropical and sub-

tropical areas (e.g., *Spirulina* is produced in Israel and Mexico, and *Chlorella* spp. have been used as food in Japan). The fouling of water systems by algae can be a problem in industrial processes, swimming pools, and reservoirs.

Algal oxidation pond: *See* Oxidation pond.

Algicides: Chemical agents that selectively kill algae.

Alginate: A polysaccharide comprising D-mannuronic and L-guluronic acids. Traditionally it has been produced from marine algae (e.g., *Laminaria* spp. and *Macrocystis pyrifera*), but the source is subject to considerable variation. Alginate is also produced commercially from *Azobacter vinelandii*, but this microbial source differs from the algal source in having *O*-acetyl groups associated with D-mannuronic acid residues. Alginates are used as thickening and gelling agents in dairy products and in textile printing, and alginate gels have been used to immobilize cells and microorganisms by entrapment.

Alkaline phosphatase (E.C. 3.1.3.1.): An enzyme (esterase) usually isolated from *Escherichia coli* or calf intestinal tissue, which hydrolyzes phosphate esters and has an optimum pH in the range 9–11. It is used in genetic engineering methodology to remove phosphate groups from 5′ termini of linear DNA molecules (e.g., a restricted plasmid molecule). This prevents recircularization of the restricted plasmid molecule by ligase during gene cloning experiments, thus ensuring that the intact circular molecules generated by the ligase contain an inserted gene.

Alkaline proteases: A general term for proteases with an optimum pH in the range 8–11. Industrially important alkaline proteases are produced from *Bacillus* spp., especially *Bacillus licheniformis*, which produces the enzyme *Subtilisin Carlsberg* (E.C. 3.4.21.14.), one of the major constituents of enzyme detergents. Alkaline proteases are used in washing powders and for dehairing hides.

Alkaloids: A nonspecific term for a range of naturally occurring organic compounds that possess marked pharmacological activity (not necessarily beneficial) in humans. Many are found in plants, and a number have found use in drug treatment (e.g., atropine, colchicine,

morphine, quinine, and scopolamine). Other alkaloids include cocaine, caffeine, nicotine, opium, and strychnine.

Allele: Any of one or more alternative forms of a given gene. They occur by mutation, where deletions, substitutions, or insertions have altered the original specific sequence of nucleotides. In a diploid cell or organism, the two alleles of a given gene occur in corresponding positions (loci) on a pair of homologous chromosomes. If these alleles are genetically identical, the cell or organism is said to be homozygous. If they are genetically different, it is heterozygous with respect to that gene.

Ambident anions: Groups of atoms carrying an overall negative charge that are capable of donating electrons to a metal atom or other electron acceptors; for example, the thiocyanate ion: S—C═N (S-bonded); S═C═N (N-bonded).

Ambident ligands: Ligands that are capable of electron donation through more than one site; for example, NH_2CH_2COOH (glycine) can coordinate either via O or N.

Aminoglycoside antibiotics: A group of microbially produced antibiotics that contain an amino sugar, an amino- or guanido-substituted inositol ring, and one or more residues of other sugars. They are all bacteriocidal. They are broad-spectrum antibiotics that function by binding to bacterial ribosomes, thus inhibiting protein synthesis, but their toxicity limits their use in the clinic. Compounds include gentamicin, kanamycin, neomycin, and streptomycin.

6-Aminopenicillanic acid (6–APA): The basic penicillin nucleus and, therefore, an important substrate for the generation of a range of clinically important penicillin analogues. It is produced industrially by the hydrolysis of penicillin G, by using organisms that produce penicillin acylase or by using immobilized penicillin acylase.

Ammonium sulfate precipitation: The use of ammonium sulfate to "salt out" proteins from solution. Precipitated proteins are collected by centrifugation. The method is often used as an initial fractionation step in the purification of proteins. Other salts, or polymers such as polyethylene glycol, can also be used. *See also* Salting-out.

Amperometric sensors: A type of electrochemical sensor in which the output from the device is in the form of an electric current that is proportional to the concentration of the analyte.

Ampholyte: An amphoteric electrolyte; a molecule that carries a net charge that will vary with the pH of the surrounding environment until at a particular value, the isoelectric point, the net charge is zero. A series of these compounds may be used to establish a pH gradient in a supporting gel for isoelectric focusing techniques.

Ampicillin: D(−)-α-aminobenzyl penicillin. A clinically important antibiotic produced from penicillin G in a two-step process. Penicillin G is hydrolyzed to 8-aminopenicillanic acid by a mutant of *Kluyvera citrophila*, after which a mutant of *Pseudomonas melanogenum* is added to the fermentation, together with the methyl ester of DL-phenylglycine, resulting in the formation of ampicillin.

Amplification (of plasmids): Increase in the copy number of a plasmid in a bacterial culture. Some multicopy plasmids (i.e., plasmids with high copy numbers, 20 or more) are able to replicate in the absence of protein synthesis, whereas the replication of genomic DNA is reliant on protein synthesis. Once sufficient bacterial cell density has been achieved, an inhibitor of protein synthesis (e.g., chloramphenicol) is added to the culture and incubation is continued for a further 12 hours. During this time, plasmid molecules continue to replicate in the absence of chromosomal replication and cell division, resulting in plasmid copy numbers often of many thousands. This method is used to increase the level of multicopy plasmids prior to plasmid isolation.

α-Amylase (E.C. 3.2.1.1.): An enzyme (endoamylase) that cleaves internal α-1,4 glucosidic bonds of starch (amylose and amylopectin) to yield oligosaccharides of varying chain length. Thermostable α-amylases exist, e.g., from *Bacillus amyloliquefaciens* and *Bacillus licheniformis*. The latter is used in the high-temperature liquefaction of starch, being capable of operating at temperatures above 100 °C. Other sources of the enzyme include bacteria or fungi such as *Bacillus subtilis* or *Aspergillus oryzae*, both of which produce the enzyme extracellularly. The enzyme has a wide range of uses, including starch degradation in baking, saccharification in brewing (mashing) and corn syrup production (starch hydrolysis), the production of low-carbohydrate beer, in wallpaper removers, in the preparation of cold-soluble laundry starch, for desizing fabrics, and as an aid to digestion. *See also* Starch.

β-Amylase (E.C. 3.2.1.2.): An enzyme with exo-α-1,4-glucanase activity. It acts on linear α-1,4-linked glucans, cleaving alternate bonds from the nonreducing end of the chain to form maltose. When amylopectin or glycogen is the substrate, the action of the enzyme is halted at α-1,6 branch points, thus producing maltose and limit dextrins. The enzyme, common in plants but rare in microorganisms, is prepared from germinating barley.

Amyloglucosidase: *See* Glucoamylases.

Amylopectin: *See* Starch.

Anaerobe: A microorganism that grows in the absence of molecular oxygen.

Anaerobic: Descriptive of a process that takes place in the absence of oxygen, for example, corrosion. Also an adjective describing an organism that can grow in the absence of molecular oxygen.

Anaerobic bioreactor: *See* Anaerobic digester.

Anaerobic digester: A bioreactor designed for the anaerobic digestion of organic wastewaters from domestic (e.g., municipal sewage) and industrial sources. The process produces a mixture of methane and carbon dioxide (Biogas) and new microbial cells. As much as 90% of the chemical energy in the wastewater can be converted to methane. For industrial uses, the design is usually a continuously stirred tank reactor (CSTR) with an inflow and outflow. The wastewater is mixed with an appropriate anaerobic inoculum and held in the bioreactor for sufficient time to allow efficient wastewater treatment and high methane yield before being expelled and replaced by further wastewater. Batch processes tend to be used for farm-scale or small-community use.

Anaerobic digestion: The bacterial fermentation of organic matter to methane and carbon dioxide that occurs in near-absence of oxygen.

Analyte: A general term used to describe the substance being determined in an analytical procedure.

Anchorage dependence: The requirement of some mammalian cell cultures to grow as monolayers anchored to a glass or plastic substrate. Only transformed cells, hybridomas, and hemopoietic cells can

easily be propagated in suspension culture. The requirement of normal cells for anchorage dependence causes problems in the scale-up of mammalian cell culture and requires the design of vessels with large surface areas. (*See also* Roller bottles, Hollow-fiber reactor, Bead-bed reactor.) However, where possible, suspension culture is the preferred method for scaling up mammalian cell culture. *See also* Suspension culture, Microcarrier.

Aneuploid: Refers to cells where there is an abnormally high or low number of chromosomes, with the individual chromosomes not in their normal proportions. *See also* Ploidy.

Animal cell culture: The large-scale growth of mammalian cells for the production of protein products. Mammalian cells are generally fragile, and fermentors designed for the growth of microorganisms are often unsuitable for growth of mammalian cells. Fermentor designs for animal cell culture are of two basic types: 1. cells are either immobilized or trapped and then perfused with culture medium; or 2. cells are in free suspension, but mixed and aerated by a very gentle technique. An airlift fermentor for the latter type has been designed, whereas hollow-fiber cartridges, roller bottles, bead-bed reactors, the encapsulation of cells in alginate spheres, and static maintenance reactors are methods used for the growth of trapped or immobilized cells. *See also* Microcarrier.

Anionic surfactant: A detergent with a negatively charged functional group. They are often alkyl or alkaryl sulfonates, for example, sodium dodecylbenzenesulfonate. *See also* Surfactants.

Anisotropic membrane: A membrane having different physical characteristics on each side (e.g., a polymeric ultrafiltration membrane having a very fine pore size on one face and an open structure on the other).

Annealing: The association of two single-stranded nucleic acid molecules by hydrogen bonding between complementary bases on the respective strands.

Anoxic reactor: A reactor used for effluent treatment in which no dissolved oxygen is present and biochemical oxidation occurs by aerobic bacteria that use nitrate ions as the oxygen source.

Antagonism: The interaction of substances such that one partially or completely inhibits the effect of the other, or even reverses the initial effect. *Compare with* Synergism.

Anther culture: A technique in which immature pollen is induced to divide and generate tissue, either on solid media or in liquid culture. Anthers containing pollen are simply removed from the plant and placed on a culture medium, where some microspores survive and develop. The generated tissue can be either embryo tissue, in which case it is transferred to an appropriate medium to allow root and shoot development to take place, or callus tissue, in which case the tissue is placed in an appropriate solution of plant hormones to induce the differentiation of shoots and roots.

Anthropogenic: *See* Xenobiotic.

Antibody: An immunoglobulin present in the serum of an animal and synthesized by plasma cells in response to invasion by an antigen, conferring immunity against later infection by the same antigen.

Antibiotic: A substance produced by a living organism that inhibits the growth of, or kills, another living organism. Many such compounds, particularly from *Streptomycetes* spp., have found use in treatment of microbial disease in humans. *See also* Cephalosporins, Penicillin G.

Antibiotic resistance: Biochemical or structural resistance to antibiotics within a microbial population. Such resistance may arise due to natural resistance, by mutations occurring within a sensitive population, or by transfer of genetic resistance factors to sensitive microbial cells. The changes enable the microorganism to grow in the presence of a specific antibiotic. For example, many microorganisms are resistant to β-lactam antibiotics because they synthesize a β-lactamase enzyme.

Anticipatory control: A system for controlling a continuous process in which control is exercised predictively rather than retroactively (feedforward rather than feedback). This type of control system requires an accurate predictive model of the process or its environment to enable precise control of the process, so that corrective action can be taken and deviation from the prescribed conditions anticipated. *See also* Feedback control, Feedforward control.

Antifoam agents: Surface-active agents used to reduce surface tension of foams formed on the surface of broths as a consequence of aeration in fermentations. The compounds most suitable for use include stearyl and octyl decanol, cottonseed oil, linseed oil, soybean oil, silicones, sulfonates, and polypropylene glycol. Their presence

can sometimes cause problems with downstream processing of the resulting products because of their surface-active nature.

Antigen: A molecule that is capable of stimulating the production of neutralizing antibody proteins when injected into a vertebrate. Antigens are usually of high molecular weight and can be purified molecules (e.g., protein, carbohydrates) or surface molecules on invading organisms such as bacteria, fungi, and viruses.

Antigenic determinant: *See* Epitope.

Antigenicity: The potential of an antigen to stimulate an immune response in a particular host.

Antioxidant: A substance that prevents or reduces oxidation, especially of organic material. The mode of action depends on the actual oxidation mechanism involved. Thus, a wide range of chemicals can be effective either by being more easily oxidized than the product to be protected, or by deactivating catalysis for the oxidation reaction, e.g., by sequestering active metals that may be present. Examples are long-chain phenols, vitamin C, and esters of hydroxyacids (propyl gallate). *See also* Glucose oxidase.

Antiserum: A serum sample containing antibodies against a specific antigen. Because most antigens have a large number of epitopes, an antiserum will contain many different antibodies against a given antigen, each antibody having been produced by a single clone of plasma cells. Such an antiserum is therefore referred to as a polyclonal antiserum. *Compare with* Monoclonal antibody.

6-APA: *See* 6-Aminopenicillanic acid.

Apical dominance: The phenomenon where axillary bud growth is suppressed in the presence of a terminal bud on a branch.

Apoenzyme: *See* Cofactor.

Apparent viscosity: The ratio of shear stress to shear rate in a fluid, when this ratio is dependent on the rate of shear.

Aqueous two-phase partitioning systems: *See* Two-phase aqueous partitioning.

ARS elements: *See* Autonomously replicating sequences.

Ascitic tumor: A tumor growing in fluid in the peritoneal cavity of a mammal. Hybridoma cells are often grown as ascitic tumors as a means of producing monoclonal antibodies.

Ascocarp: A fungal fruiting body of an Ascomycete, which bears or contains asci. *See also* Ascus.

Ascomycete: A fungus belonging to the Ascomycotina, the largest fungal subdivision, with over 15,000 known species. Classified on the basis of the production of ascospores within an ascus.

Ascospore: The sexual spore of an Ascomycete (fungus), borne in an ascus.

Ascus: A spherical or cylindrical saclike structure, produced by Ascomycetes (fungi), which contains a definite number of ascospores. The number of spores is normally eight, but in certain cases is some other multiple of two.

Asepsis: Freedom from contamination by undesirable or harmful microorganisms.

Aseptic technique: Precautionary measures taken in microbiological work and clinical practice to prevent the contamination of cultures or sterile media and the infection of persons by extraneous microorganisms.

Asexual: Reproduction, either vegetative or involving spore formation, that occurs without fusion of two nuclei (sexual).

Asexual propagation: *See* Vegetative propagation.

Aspartame: A synthetic dipeptide ester, L-asp-L-phe-OMe, *N*-L-α-Aspartyl-L-phenylalanine methyl ester, used as an artificial sweetener; about 200 times as sweet as 4% sucrose in aqueous solution. It is synthesized by the condensation of *N*-benzyloxycarbonyl-L-aspartic acid with L-phenylalanine methyl ester, followed by removal of the *N*-benzyloxycarbonyl group. The condensation is catalyzed by thermolysin under conditions that encourage the equilibrium toward peptide bond synthesis rather than the hydrolysis of peptide bonds. Metalloproteases such as thermolysin are particularly useful for this type of synthesis because, unlike most other proteases, they do not have esterase activity.

L-Aspartic acid: An amino acid ($HO_2CCH_2CH(NH_2)CO_2H$) widely used in medicine (e.g., for treating cramps, liver disease, and anemia), foods (as a seasoning), and cosmetics. Produced commercially by the fermentation of fumaric acid, or from fumaric acid and ammonia by using immobilized microbial cells with high aspartase activity. The introduction of the sweetener, aspartame, has increased the demand for aspartic acid.

Aspect ratio (of fermentors): A term used for the height-to-diameter ratio of a tower fermentor.

***Aspergillus* spp.**: A genus of filamentous fungi belonging to the Deuteromycotina. The fungi are normally easy to grow and produce a wide range of enzymes and metabolites. *Aspergillus niger*, for example, is used for the industrial production of citric acid, gluconic acid, amylase, proteases, glucose oxidase, and pectic enzymes.

Association: Combination of molecules to produce larger, more complex, species. Often used in relation to liquids. In an associated liquid the molecules are linked by weak chemical bonds (hydrogen bonds). This weak linkage produces physical properties that are anomalous when compared with nonassociated liquids. Typical examples are water and low-molecular-weight alcohols.

Atropine: An anticholinergic compound isolated from the plant *Atropa belladonna*.

Autoanalysis: A term given to a range of analytical techniques that can be adapted to provide automatic sampling and quantitative analysis. The instruments often involve a continuous flow of liquids through small-bore tubing with manifolds for mixing of reagents, dialysis, and liquid–liquid extraction, coupled to suitable detectors (e.g., colorimetric, fluorescent, or electrolytic) equipped with flow-through cells and automatic printout of results.

Autoclave: An apparatus in which objects or materials may be sterilized by air-free saturated steam (under pressure) at temperatures in excess of 100 °C. Water is heated in a closed system (with appropriate pressure-release valves) to generate steam temperatures suitable for sterilization (e.g., 121 °C). The smallest and simplest form of autoclave, commonly used in laboratories for sterilizing small samples, is the domestic pressure cooker.

Autolysis: The process of self-digestion of cellular components ef-

fected by enzymes naturally present in tissues or microorganisms, usually following the death of the cell or tissue.

Automatic cell counter: *See* Coulter counter.

Autonomously replicating sequences: Chromosomal sequences with the ability to allow autonomous replication of plasmids in yeast. Such sequences have been isolated from many regions of the yeast genome and other eukaryotic species. They were thought to be chromosomal origins of replication, but may only fortuitously act as such in yeast. *See also* Yeast replicative plasmids.

Autoradiography (radioautography): The process whereby a photographic film is used to locate radioactively labeled substances, e.g., radiolabeled DNA bands on a gel. The specimen is overlayered with a photographic film and left for a length of time determined by the amount of radioactivity present. When the film is developed, an image is produced that indicates the location of the radioactive sample.

Autotrophs: Organisms that use environmental CO_2 as their carbon source. They include green plants, algae, and various bacteria. *Compare with* Heterotrophs. *See also* Photoautotrophs, Chemoautotroph.

Auxins: A group of endogenous plant-growth substances, chemically related to indoleacetic acid (IAA), which is itself the principal auxin of many plants. They are characterized by their ability to promote plant growth by processes such as cell elongation and root initiation. Among the auxins commonly used in plant cell and tissue culture are 1-naphthaleneacetic acid (NAA) and 2,4-dichlorophenoxyacetic acid (2,4-D).

Auxochrome: A group of atoms attached to a chromophore that modifies the light absorption of the latter.

Auxotroph: A mutant microorganism that will grow only in the presence of a nutrient not required by the wild-type form of the microorganism (e.g., histidine auxotrophs require histidine for growth).

Avidin: A glycoprotein (MW 67,000) found in egg white that binds to the vitamin, biotin, with very high affinity ($K_D = 10^{-15}$ M). Both proteins and nucleic acids can be linked to biotin (biotinylated). The high affinity between avidin and biotin is used to amplify the identification

of interactions such as antigen–antibody reactions or the hybridization of DNA strands. For example, a biotinylated DNA probe will hybridize to complementary DNA on a filter. The presence of this biotinylated DNA is detected by treatment of the filter with avidin linked to a marker enzyme such as horseradish peroxidase (HRP), followed by the addition of a substrate for HRP that is converted to a colored product by the enzyme. The production of color indicates the position of the biotinylated DNA. Because protein and DNA can have many biotin molecules bound to one molecule, many avidin molecules can bind to one biotinylated molecule, thus considerably amplifying the signal.

Avidity: The net combining power of an antibody molecule with its antigen.

Axenic culture: A microbial culture that contains only one species of organism.

Axial mixing: In fluid flow, the phenomenon by which elements of the fluid are either retarded (back mixing) or accelerated (forward mixing) relative to the average retention time. Axial mixing tends to affect both reactor efficiency and throughput; it is generally regarded as a disadvantage to processing. *See also* Plug flow, Back mixing, Forward mixing.

Azeotropic distillation: A method for separating the components of an azeotropic mixture. When an azeotropic mixture is formed, it is impossible to separate the components of this mixture by fractional distillation. However, if a third component is added such that the added liquid forms azeotropic mixtures with the original two components, two new azeotropic mixtures are formed that can now be separated from each other by distillation.

Azeotropic drying: A process whereby water can be removed from a liquid by the addition of a second liquid that forms an azeotropic mixture with the water, thereby allowing the removal of water at a lower temperature than 100 °C.

Azeotropic mixture: A mixture of liquids in which the composition of the vapor is the same as the liquid phase. Thus, the mixture distills without change in composition. Also called constant boiling mixture.

Azide: *See* Sodium azide.

***Azotobacter* sp.**: Large oval pleomorphic Gram-negative bacteria that are obligate aerobes and able to fix atmospheric nitrogen in the presence of carbohydrates or other energy sources. They are cultured on a large scale, to be used as soil inocula or as seed dressings. *See also Rhizobium*.

Bacillus: A genus of Gram-positive rod-shaped bacteria that produce endospores. Some species are used for the large-scale production of amylases, proteases, and microbial insecticides. Because of the heat resistance of the spores, *Bacillus* strains are a common source of contamination.

Bacillus popilliae: This bacterium, which attacks only the Japanese beetle (*Popillia japonica*), has been used for control purposes in the United States. The infected beetle larvae become milky white because of bacterial spore production in the hemolymph.

Bacillus subtilis: A Gram-positive, spore-forming, rod-shaped bacterium that is nonpathogenic in humans and animals. Because of the considerable knowledge of the genetics of this organism and its ability to secrete considerable amounts of protein, it is much used as a vehicle for genetic engineering. Both phages and plasmids will replicate in *B. subtilis.*

Bacillus thuringiensis: A Gram-positive bacterium with potential for improving disease resistance in plants. Resting spores of the bacterium contain crystalline protein inclusion bodies (δ-endotoxins) that are toxic against a variety of insects. Various strains of *B. thuringiensis* differ in their spectra of insecticidal activity. Most are active against Lepidoptera, but some strains specific to Diptera and Coleoptera have

been identified. Both preparations of the endotoxins and spores from *B. thuringiensis* have been produced as pest-control agents. Genes for the toxic proteins have also been cloned, and the transfer of these genes to plants is being investigated. For example, transgenic tobacco plants have been developed that express one of these toxin genes and synthesize insecticidal protein. These plants have been shown to be protected from feeding damage by tobacco hornworm larvae.

Bacitracins: Branched, cyclic antibiotic peptides active against Gram-positive bacteria, produced by strains of *Bacillus licheniformis*.

Backflushing: The reversal of a process against the normal service flow, so as to dislodge particulate material. This allows the cleaning of a column of adsorbant, membrane, or filter.

Back mixing: In fluid transport, the phenomenon where some elements of the fluid are retarded relative to the average element and thus have a higher residence time in the reactor or pipe. This leads to a reduction in throughput of the system. *See also* Axial mixing, Forward mixing.

Back mutation: A mutation that causes a mutant gene to regain its wild-type function.

Backwashing: *See* Backflushing.

Bacteriocide: A compound capable of killing bacteria (e.g., bactericidal, germicidal).

Bacteriophage: Normally referred to as "phage." Any virus that specifically infects a bacterial cell. Such viruses comprise a protein coat (capsid) surrounding genetic material (normally DNA, but sometimes RNA) that is injected into the cell on infection. Bacteriophages are used in genetic engineering as a means of introducing new genetic material into a cell (i.e., they are used as vectors). *See* λ-Phage, M13. *See also* Lysogenic infection.

Bacteriophage M13: *See* M13.

Bacteriostatic: Capable of inhibiting bacterial growth, but not of killing the cells.

Baculovirus: A group of viruses that infect only arthropods, (spiders, crabs, insects, millipedes, centipedes, etc.). This selectivity, and in particular the fact that they do not infect vertebrates, has led to their being investigated as potential pest-control agents.

Bagasse: The fibrous part of the sugar cane stem, essentially lignocellulose, that remains when the juice has been extracted. It is generally burned to supply energy for crushing more canes or to distill alcohol produced by fermentation of the sugar juice, but it is also used as cattle feed and in the preparation of paper and film board.

Bakers' yeast: The pressed yeast (*Saccharomyces cerevisiae*) that is grown specifically for use in baking. The culture is grown under stirred aerobic conditions with controlled addition of nutrients in stages to produce maximum biomass and minimum alcohol.

Bal 31: An exonuclease, isolated from *Brevibacterium albidum*, that cleaves both the 5′ and 3′ strands from both ends of a DNA duplex. It forms a shorter DNA molecule, the size of which is determined by the time of digestion. The enzyme is used to make deletions in cloned DNA molecules.

Ball mill: Device used for the crushing and grinding of materials. It consists of a drum rotating about a horizontal axis. The drum contains a number of hardened balls that crush the material by attrition, either between themselves or between the side of the drum and the balls.

BAP: Abbreviation for bacterial alkaline phosphatase. *See also* Alkaline phosphatase.

Base pairs (bp): The formation of hydrogen bonds between adenine (A) and thymine (T) or between guanine (G) and cytosine (C) bases in a DNA molecule. There are two hydrogen bonds in an A–T base pair and three in a G–C base pair. Such base pairing is responsible for maintaining the double-stranded form of DNA. The size of a DNA molecule is normally referred to in terms of the number of base pairs (or thousands of base pairs, kbp), rather than the absolute molecular weight, which is normally a large and unwieldy figure. Some writers abbreviate kbp to kb when referring to the size of DNA. If base pairing is disrupted, the DNA is said to be denatured or melted.

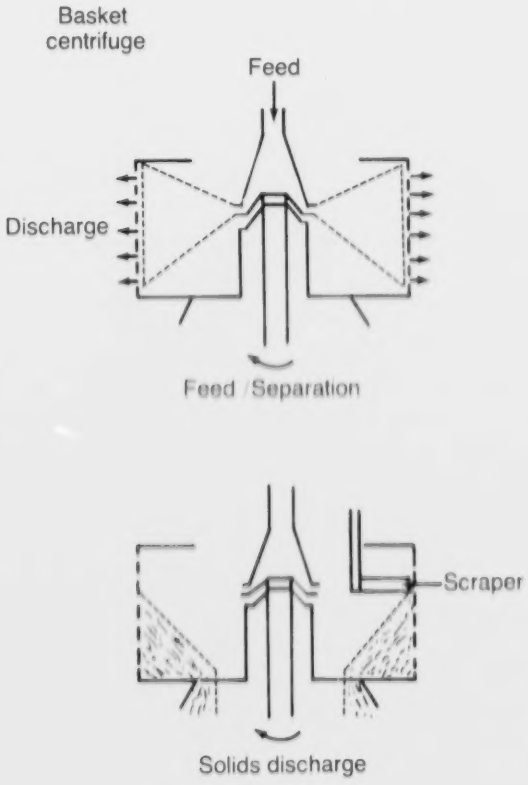
Basidiocarp: A fungal fruiting body of a basidiomycete, which bears or contains basidia. *See also* Basidium.

Basidiomycete: A fungus that belongs to the Basidiomycotina, a group of approximately 3000 species. This group includes many of the large toadstools, as well as microfungi and plant pathogens. These fungi produce basidia and basidiospores.

Basidiospore: The sexual spore of a Basidiomycete (fungus), borne on the outside of a basidium as a result of karyogamy and meiosis.

Basidium: A short clublike cell produced by Basidiomycete (fungi). It bears four tiny projections (sterigmata), on each of which a spore is borne. Two nuclei fuse in the basidium; the fusion gives rise to four daughter nuclei that go into each developing spore.

Basket centrifuge: A centrifuge design in which the bowl or basket is perforated to allow passage of the filtrate and is lined with some form of filter cloth to retain the solids. Thus the centrifuge operates



essentially as a centrifugal filter and is used to collect solid matter. It operates at low rotational speeds, about 1000 rpm. The disadvantages of the basket centrifuge include the need for batch operation and a low capacity for solids, typically about 10 kg.

Batch culture: A fermentation process in which all the necessary materials, with the exception of oxygen for aerobic processes, are placed in the reactor at the start of the operation. The fermentation is allowed to proceed until completion, at which point the product is harvested. *Compare with* Continuous culture.

Batch process: A discontinuous process whereby a single loading of the reactor, etc., is allowed to proceed to completion and then discharged before there is any further addition of reactants. *Compare with* Continuous processing.

Bathochromic shift: The movement of a characteristic spectral band to longer wavelength, lower frequency, or lower energy following the insertion of a substituent into the molecular structure. Converse of hypsochromic shift.

Bead-bed reactor: A reactor design for the large-scale growth of mammalian cells. Cells are grown on the surface of glass beads (3–5-mm diameter) packed in a glass column, through which medium is continually pumped. When growth is confluent, cells can be recovered by trypsin treatment.

Bead mill: A device for the rupturing of cells by using a ball-type mill loaded with glass or ceramic beads. These mills are available for both laboratory and large-scale processing. The former include the Mickle tissue disintegrator and Braun homogenizer. A major disadvantage of these mills is the increase of sample temperature during disruption. Devices are, however, available that incorporate cooling jackets. The large-scale units incorporate both glass beads and rotating discs in the grinding chamber. The suspension of cells is disrupted by collisions between shear force layers generated by the high-speed rotation of the discs and also by grinding of the glass beads. A number of designs are available with varying geometries of the agitator discs and orientations of the grinding chamber. One problem with this type of disintegrator is the possibility of denaturation, apparently caused by the shear forces and local heating effects.

Bed volume: The total volume occupied by the support material in a chromatographic column. Also a unit of volume for fluids used in

processing such columns. Sometimes called column volume. *See also* Void volume.

Beer–Lambert law: A law relating the adsorption of radiation passing through an absorbing fluid with the thickness (path length) of the fluid and the concentration of the absorbing substance. This law allows the determination of the concentration of substances in solution and applies to many spectrophotometric systems, in particular to ultraviolet and visible radiation. The law may be represented by the equation:

$$A = kcl$$

where A is absorbance, c is concentration, l is path length, and k is a constant, the absorption coefficient. Various units may be used, but the SI units require c in moles per cubic meter; l in meters; because A is dimensionless, k has the units square meters per mole. *See also* Absorbance, Absorption coefficient, Isosbestic point.

Beet molasses: The concentrated liquor remaining after crystallization of the sucrose from beet sugar solutions. It contains approximately 48% w/v sucrose, 1% w/v raffinose, and 1% w/v invert sugar. The remainder is noncarbohydrate.

Belt press–filter: A mechanical device for filtering–dewatering of slurries, broths, etc. The feed is passed between two endless belts rotating continuously under tension, thus squeezing out the contained liquid. An alternative design squeezes the slurry between an endless belt and a perforated drum. A belt filter differs from a belt press in that it is a vacuum device.

Benzylaminopurine: *See* Cytokinins.

Benzylpenicillin: *See* Penicillin G.

Berberine: A yellow isoquinoline alkaloid found in several plants, including *Coptis japonica*, *Phellodendron amurense*, and *Thalictrum rugosum*. It is used as an intestinal antiseptic in Japan. The production of berberine by cell culture is currently being investigated.

Beta-: Compounds beginning with β- are listed under their Roman names.

BET isotherm: An adsorption isotherm based on a theory by Bru-

nauer, Emmett, and Teller concerning multilayer adsorption onto a surface. The authors postulated a number of simultaneous Langmuir-type adsorptions between each two successive molecular layers. The expression for the BET isotherm for gas adsorption has the form

$$V = \frac{V_m C_p}{(p_o - p)[1 + (C - 1)(p/p_o)]}$$

where V is volume of gas adsorbed at pressure p, V_m is monolayer capacity of the substrate, p_o is saturated vapor pressure of gas, and C is constant for any given gas. Similar equations can be deduced for other adsorbed fluids.

Bingham equation: A linear equation relating to plastic fluid flow of liquids such as may be found in fermentation broths. These fluids follow the equation:

$$\tau = k\gamma + \tau_o$$

where τ is the applied stress, γ is the shear rate, and τ_o is the yield stress. A fluid that follows this equation is termed a Bingham plastic or Bingham fluid. An example of this behavior is found with kanamycin fermentation using *Streptomyces kanamyceticus*, and also with penicillin G fermentation using *Penicillium chrysogenum*.

Bingham plastic: *See* Bingham equation.

Binodal curve: A curve denoting the limiting values of concentrations at which a single phase is transformed into two phases. For instance, with fluids that are partially miscible, there is a range of concentrations over which two phases are formed.

Bioaffinity chromatography: *See* Affinity chromatography.

Bioaffinity sensor: A biosensor in which molecular recognition is used to generate the biochemical signal. Thus immobilized hormone receptors, drug receptors, or antibodies can be used to detect hormones, drugs or drug metabolites, or antigens, respectively.

Bioassay: Any method for determining the concentration or activity of a substance by measuring its effect on a living organism.

Biocatalyst: A catalyst that is, or is derived from, a living organism, a tissue sample, or cell culture. *See also* Enzyme immobilization, Cell immobilization.

Biochemical fuel cells: Any system that uses biological reactions to effect the conversion of fuel or biomass (chemical energy) to electricity (electrical energy). The ultimate aim is to be able to generate electricity from any form of industrial waste or sewage. Commercially available cells exist, but they have yet to be evaluated for routine practical uses.

Biochemical oxygen demand (BOD): A measure of the quantity of oxygen required for microbial oxidation of organic matter in water. Samples are incubated in the dark for 5 days at 20 °C, and the oxygen consumed is measured in milligrams per cubic decimeter of sample. BOD is often used as a measure of the extent of organic pollution of water. *See also* Chemical oxygen demand.

Bioconversion: *See* Biotransformation.

Biodegradable: Referring to compounds capable of being broken down by living organisms.

Biodeterioration: Any undesirable changes in the properties of a material brought about by the activities of organisms. It is a very broad term that covers a wide range of situations, including microbial corrosion of stone and metal, mold and bacterial growth on leather products, microbial degradation of rubber and plastics, fungal growth in aviation fuels and oils, wood-rotting, the breakdown of lubricants by microorganisms, crop damage by microorganisms, blocking of pipes by microbial growth, staining of materials by microbial contamination, and the growth of microorganisms in foodstuffs.

Biofilm: An actively growing pure or mixed microbial population irreversibly adhering to a living or nonliving surface. Adhesion is mediated by microbial production of polysaccharides and glycoproteins. Biofilms cause biofouling in industrial water systems. This fouling leads to to corrosion, increased power consumption, and structural damage to cooling towers. Aerosols produced in air-conditioning plants may contain *Legionella* sp. Biofilms are also important in sewage filter beds (*see also* Percolating filter) and in some cell-immobilization techniques.

Biofilter: A type of filter consisting of a tank filled with a solid material on which an active biomass is supported. The biomass reduces the organic content of the water, as well as removing particulate matter. Often used for wastewater treatment.

Biofuel: Any fuel obtained from biological raw materials or by biological processing. The major biofuels are biogas produced by anaerobic digestion and ethanol produced by the fermentation of sugar, molasses, or hydrolyzed starch.

Biofuel cells: *See* Biochemical fuel cells.

Biogas: A mixture of methane and other gases (primarily carbon dioxide) produced by anaerobic fermentation of organic matter such as sewage or agricultural byproducts. The methane concentration is usually between 50% and 70%. The gas can be used either directly for cooking or lighting, or as a raw material in the production of other compounds. The methane concentration can be enriched by removing the remaining gases and then used to power engines. In many rural areas in underdeveloped countries, biogas provides a major source of energy.

Biogenic: *See* Xenobiotic.

Biological control: The deliberate use of one species of organism to control or eliminate another. Biological control utilizes the fact that certain microorganisms can inhibit the growth of others by either antagonistic or competitive mechanisms. One microorganism can therefore be used to control a different microbial population. For example, inoculation of the fungus *Trichoderna lignorum* into wet soil suppresses damping off of seedlings. This fungus produces a toxin that kills other fungi involved in the damping-off process. *See also Bacillus thuringiensis*, Nuclear polyhidrosis virus, *Verticillium lecanii*.

Biological oxygen demand (BOD): A measure of the amount of oxygen taken up as a result of microorganism respiratory activity in water samples. The sample is incubated at 25 °C for a fixed time, often five days, and the amount of oxygen removed from the sealed system is determined. The result, expressed in milligrams of oxygen per cubic decimeter of water, is termed the BOD and serves as an indicator of water pollution; the higher the value, the greater the pollution. Also termed biochemical oxygen demand.

Bioluminescence: The emission of visible light by living organisms. It is achieved by the oxidation of an ATP–luciferin complex by the enzyme luciferase. This process is used as the basis of a sensitive assay for ATP, using the luciferase–luciferin complex of the firefly.

The sensitivity of the assay allows it to be used for the identification and quantitation of populations of microorganisms.

Biomass: A general term to describe purposely grown plants or biological wastes, such as those produced from agriculture or food processing, that are available for conversion by biotechnological processes to high-grade fuels and speciality chemicals. More specifically, in microbiology, the cellular component of a biotechnological process (e.g., the bacteria in a fermentation process). It may either be an unwanted waste product, the required product (e.g., single-cell protein), or a source of the required product (e.g., an intracellular product such as an enzyme).

Biophotolysis: The use of the photosystems of photosynthetic organisms to cleave water into hydrogen and oxygen, which can then be used as an energy source.

Biopolymer: A broad term that covers many large-molecular-weight compounds (e.g., polysaccharides, nucleic acids) that are produced from biological sources. However, in terms of commercial usage, the most important biopolymers are polysaccharides. *See also* Xanthan gum, Dextran, Alginate, Zanflo, Polytran.

Bioprobe: *See* Biosensor.

Bioreactor: A containment vessel for biological reactions, used in particular for fermentation processes and enzyme reactions. Bioreactors are normally constructed of stainless steel and have such features as provision for inoculation and sampling, variable aeration (for aerobic processes), variable agitation, and temperature control. For fermentation processes it must be possible to sterilize the system and operate under sterile conditions, as well as to fill and empty the system aseptically. Also, the design should allow the operator to monitor and optimize growth and product formation. Various designs are available, including continuous stirred tank reactors, tower bioreactors, loop (recycle) bioreactors, anaerobic digesters, activated sludge processes.

Bioscrubbing: The removal of toxic or odorous wastes using biological systems, particularly microorganisms. Many industrial processes produce toxic or odorous gases, particularly reduced sulfur compounds such as hydrogen sulfide, dimethyl sulfide, and mercaptans, and toxic wastes such as cyanide, many of which can be smelled by humans at very low concentrations (ppm or ppb levels). The malodors

of animal wastes are due to reduced sulfur compounds. The scrubber compartment is often a spray column in which finely distributed water droplets flow countercurrently to the waste gas. This results in a continuous mass transfer of pollutants and oxygen from the waste gas to the liquid phase. Oxidative reactions using microorganisms then take place in the aqueous phase. Many potential uses of microorganisms for scrubbing exist, such as anaerobic desulfurization using *Thiobacillus* spp. and the conversion of cyanide to thiocyanate by rhodanase, an enzyme found in *Bacillus stearothermophilus*. However, these systems have not yet been fully developed for wide-scale application.

Bioselective chromatography: *See* Affinity chromatography.

Biosensor: An analytical tool or system consisting of an immobilized biological material (e.g., enzyme, antibody, whole cell, organelle) in intimate contact with a suitable transducer device that will convert the biochemical signal into a quantifiable electrical signal. A wide range of biosensor devices has been described, based on a number of different transducer systems, including conductimetric, redox mediated, field-effect transistor, thermistor type, optoelectronic devices, photodiodes, fiber optic devices, gas-sensing electrodes, piezoelectric crystals, and ion-selective electrode systems. Biosensors have advantages over physicochemical sensors, but they currently suffer from a short working lifetime. Also, it is not possible to autoclave biosensors.

Biospecific adsorption chromatography: *See* Affinity chromatography.

Biostat: A continuous-culture vessel in which a parameter other than turbidity is used to monitor the biomass concentration.

Biosurfactant: Any compound produced by a living organism that solubilizes compounds (e.g., oils) by reducing the surface tension between the compound and water.

Biotin: A water-soluble vitamin (MW 244) that is very tightly bound by avidin ($K_D = 10^{-15}$ M). This high affinity is used to amplify the detection of protein–protein or DNA–DNA interactions. For example, a DNA probe can be biotinylated by incorporating biotin derivatives of deoxyribonucleotides by nick translation. After hybridization the biotin can be detected by binding an avidin–enzyme complex. A substrate is then provided for the enzyme (usually peroxidase or alkaline

phosphatase), which is converted to a colored product. The color indicates the position of the biotinylated probe.

Biotinylation: The linking of biotin molecules to macromolecules such as DNA or protein. *See also* Biotin.

Biotransformation (bioconversion): The carrying out of a chemical reaction by biological systems. Reactions include reduction, oxidation, hydroxylation, epoxidation, esterification, and isomerization. Normally carried out by using enzymes, either in a purified or semi-purified state, or by whole cells (plant, animal, or microbial) that contain the relevant enzyme. For example, *Rhizopus nigricans* is used to hydroxylate progesterone at position 11 during the synthesis of the steroid cortisol.

Biotrophic fungi: Fungi that live by parasitizing living host cells.

Bis (bisacrylamide): An abbreviation used to refer to *N,N'*-methylenebisacrylamide. *See also* Polyacrylamide gels.

Blinding: The wedging of particles that are not quite small enough to pass through the pores of a filter, so that an appreciable fraction of the filter surface becomes inactive.

Blue-green algae: Photosynthetic, oxygen-evolving prokaryotes. Although referred to as blue-green algae, they are not true algae and are more correctly classified as Cyanobacteria.

Blunt end (flush end): An end of a DNA molecule where both strands terminate at the same nucleotide position with no single-stranded extension. *Compare with* Sticky ends. *See also* Restriction endonucleases.

Boundary layer: A layer of fluid in the immediate vicinity of a surface that forms a boundary between the surface and the bulk phase of the liquid. Flow in the boundary layer is laminar, and transfer of heat and mass across the layer can occur only by molecular diffusion.

Bovine papilloma virus (BPV): A DNA virus that causes warts on cattle. It has potential as a vector for transforming mammalian cells. The virus does not lyse its host cell, but replicates as a plasmid with a copy number of 10–200 per cell.

Bowman–Birk inhibitors: A group of protease inhibitors found in soybeans.

bp: An abbreviation of "base pair." Used as a measure of the size of double-stranded DNA. *See also* Base pairs.

Braun homogenizer: *See* Bead mill.

Breakthrough profile: A plot of the concentration of compounds present in the effluent of the absorption column as a function of the effluent volume. The purpose of these profiles is to provide a representation of column efficiency in the separation of mixtures of components and to assess the optimum conditions for column operation. The shape of the profile should ideally be a step function indicating that the compound being studied is passing down the column of adsorbant as a discrete band. However, because of the adsorption of compounds onto the column, partitioning is not ideal and depends upon the relevant adsorption isotherm. In addition, axial mixing occurs because of inconsistencies in column packing. An S-shaped curve is normally found for a breakthrough profile because of these problems. *See also* BET isotherm, Freundlich isotherm, Langmuir adsorption isotherm.

Brewing yeasts: The two main groups of brewing yeasts are known as "top-yeasts" (strains of *Saccharomyces cerevisiae*) and "bottom-yeasts" (*Saccharomyces carlsbergensis*). Top-yeasts, used for brewing traditional beers, tend to be carried to the surface of a vessel during fermentation and flocculate on the surface as a thick scumlike layer. Bottom-yeasts are used for brewing lagers. Comparatively longer fermentations are carried out at lower temperatures, and the yeast cells stay at the bottom of the vessel.

Broad host range: A term that describes a plasmid or phage that replicates in a range of host species or strains, rather than being specific to one host species or strain.

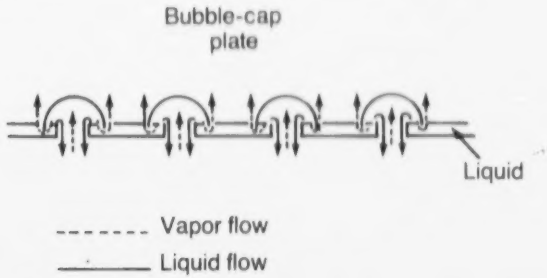
Bromelain (E.C. 3.4.22.4.): A thiol protease (MW 33,500) isolated from pineapple juice and stems. The enzyme is used in animal feeds to improve their nutritional value, as a digestive aid, as a meat tenderizer, and in chillproofing.

Broth: A term given to the content of a fermentor comprising nutrients, microorganism, substrates, primary and secondary metabolites, and supporting fluid.

Broth conditioning: The initial stage in downstream processing that occurs after the contents of a fermentor are harvested. It consists of a number of different processes designed to simplify and facilitate downstream processing and may include reduction of viscosity, ag-

gregation of solids, and increase of particle size or density. These processes lead to easier control of solids and reduction of fouling. Processes that may be involved include addition of flocculants, filter aids, pH variation, and heat treatment.

Bubble-cap plate: A device for contacting vapor or gas and liquid in distillation or adsorption columns. It consists of a series of hollow mushroomlike protrusions on a plate that direct the vapor through the absorbing liquid.



Bubble column: Any type of gas–liquid contactor where the sparge gas is the only means of agitation. *See also* Airlift fermentors.

Bubble column fermentor: High aspect–ratio fermentor with gas introduced at the base through a nozzle or porous plate. Gas bubbles rise through the medium in the fermentor and cause mixing. The bubbles may also be redispersed by a series of horizontal baffle plates set at intervals. This type of fermentor produces very little shear effect on the organism. Also called sparged tank. *See also* Airlift fermentors.

Budding: The production of a small budlike outgrowth from a parent cell. It is a method of asexual reproduction common among yeasts.

Butanol: *See* Acetone–butanol fermentation.

C*: A term used for the saturation concentration (mmol dm^{-3}) of dissolved oxygen in a fermentation broth for any given set of fermentation conditions.

Calcofluor white: A fluorescent reagent used to stain plant cell walls. Used in particular to test whether or not protoplasts have regenerated cell walls.

Calliclone: A discrete colony that derives from a single cell when plant cells in suspension culture are plated out in semisolid medium.

Callus: Plant tissue consisting of dedifferentiated cells, produced either as a result of tissue wounding in the plant or by the growth of plant tissue explants on semisolid media. *See also* Callus culture.

Callus culture: The growth of plant tissue explants on semisolid agar, giving rise to an amorphous mass of undifferentiated cells with no regular form (callus). In many cases this callus material can be induced to differentiate into whole plants (via either organogenesis or embryogenesis) by the inclusion of appropriate growth regulators (auxins, cytokinins, etc.) in the culture medium.

Calomel electrode: A type of reference electrode used with a glass electrode to measure hydrogen ion activity or concentration (i.e., pH). It consists of mercury in contact with solid mercury(I) chloride and a solution of potassium chloride, normally a saturated solution. A combined electrode is used with most modern pH meters; the glass electrode is surrounded by a concentric cylinder that contains the calomel electrode. A fiber or porous plug in the outer wall of the cylinder provides for electrical contact between the reference electrode and the surrounding liquid. These combined electrodes are capable of steam sterilization and can be used as in-line sensors for fermentors.

Cane molasses: The concentrated liquor remaining after crystallization of the sucrose from cane sugar solutions. It contains approximately 33% w/v sucrose and 21% w/v invert sugar. The remainder is noncarbohydrate.

Cane sugar: Sucrose extracted from sugar cane. It is no different from sucrose obtained from any other source, such as sugar beet.

Capillary membrane module: The arrangement of a membrane in the form of a bundle of capillaries installed in an outer shell. The mass separation layer of the polymeric membrane is on the inside of the capillary, and the feed solution is fed into the lumen. The permeate leaves the module from the outer shell. This type of module construction is used in ultrafiltration and pervaporation, as it gives a large membrane area per volume with low capital and operating costs, together with good control of polarization concentration and fouling. A disadvantage is the relatively low bursting pressure of the capillaries (about 5×10^5 Pa). Also termed a hollow fiber module.

Capsid: The external protein "coat" or "shell" of a virus particle; it surrounds the core (RNA or DNA) of the virus.

Capsomere: Any of the individual protein units that form the capsid of a virus.

Capsule: A compact gumlike layer of polysaccharide or polypeptide, exterior to the cell wall in some bacteria. Some of the gums are produced on a large scale for use as gelling agents or thickeners. *See also* Glycocalyx, *Leuconostoc*, Slime layer.

Carbon dioxide gas analyzer: An instrument for measuring the concentration of carbon dioxide in a gas stream, often the exhaust gas

from a fermentor. The detector in the instrument may be based on IR spectrophotometry, thermal conductivity, or mass spectrometry.

Carbon dioxide production rate (CPR): The change in carbon dioxide concentration in the exhaust gas from a fermentor; can be used to measure growth of cells.

Carbon source: A substance that provides the major part of the carbon requirement for a growing organism.

β-Carotene: A coloring agent used in the food industry. *See also* Carotenoids.

Carotenoids: Plant pigments, usually red or yellow, based on a tetraterpene structure. Their color results from the presence of a long series of conjugated double bonds. They are precursors of vitamin A and are thus used as food supplements. The traditional source of carotenoids is the carrot, which provides a mixture of carotenoids, with β-carotene as the major component (>90%). β-Carotene is produced commercially from a range of algae, bacteria, fungi, and yeasts. It is used as a coloring material in foods and as a source of vitamin A in vegetarian margarines.

Carrageenans: A mixture of heterogeneous polysaccharides, comprising mainly α-D-galactopyranosyl sulfate esters, isolated from seaweed. κ-Carrageenan, used in immobilizing cells, is the insoluble fraction obtained when potassium ions are added to an aqueous solution of carrageenan. Also used as a food additive and as an absorbent for metal ions.

Cascade: A type of continuous processing in which a series of identical operations like liquid–liquid extraction or solid–liquid leaching are operated so that the feed for a particular stage is the product from the previous stage. Several different configurations are possible; the choice depends on the particular requirements of the flowsheet. *See also* Cocurrent flow, Crosscurrent flow, Countercurrent flow.

Cascade fermentation: An arrangement of a series of fermentors such that the fermenting liquor is fed through the system as a cascade. Modifications are possible to retain the cells in intermediate fermentors (tanks) while the liquor is allowed to continue.

Casein: The major protein component of milk (2.6% of whole milk).

Casein is not a single protein, but a heterogeneous group of phosphoproteins. The nomenclature of the casein complex has changed continuously as research progresses, but essentially consists of three major components: α-, β-, and κ-casein, representing approximately 40%, 35%, and 15% of the total casein, respectively. Minor casein components make up the remaining 10%.

Casson body: A rheological term originally used by Casson to describe a type of non-Newtonian fluid that behaves as a pseudoplastic. The apparent viscosity decreases with increasing shear rate, but it displays a yield stress and therefore resembles a Bingham plastic.

Casson fluid: A type of non-Newtonian rheological behavior shown by some fermentation broths that can be represented by the equation:

$$\tau^{0.5} = \tau_o^{0.5} + k\gamma^{0.5}$$

where τ is applied stress, τ_o the yield stress, and γ the shear rate.

Catabolite repression: The inhibition of enzyme synthesis by increased concentrations of certain metabolic products or substrates (e.g., glucose repression of the *lac* operon).

Cation exchange: The replacement of one positively charged ion for another, often involving the use of ion-exchange resins (for example, in water softening, calcium and magnesium ions are replaced by sodium).

Cationic surfactant: Compounds that, in aqueous solution, form positively charged surface-active species. These are often derived from quaternary alkylammonium salts or derivatives of fatty acid amides (e.g., cetyltrimethylammonium chloride).

Cauliflower mosaic virus (CaMV): A member of the caulimovirus family of viruses. CaMV is of interest as a possible cloning vector in plants. It has the advantage that a single infection of a plant results in the virus being transmitted throughout the plant, with every cell becoming infected. Regeneration of plants from transformed cell cultures is therefore not necessary. However, the use of CaMV is limited, in that only small inserts can be added to the CaMV genome without interfering with the packing of the DNA into the viral protein coat. CaMV also has a very limited host range, infecting only a small number of species, primarily the brassicas.

Caulimoviruses: One of the two classes of DNA viruses (the other is geminiviruses) that infect plants. They have potential as cloning vectors in plants. *See also* Cauliflower mosaic virus.

C_{crit}: *See* Critical dissolved oxygen concentration.

cDNA: *See* Complementary DNA.

Cell culture: *See* Tissue culture.

Cell cybrids: A population of cells produced by combining the cytoplasm of one cell type with the nucleus of another cell type.

Cell-free translation system: A crude cell extract (which thus contains ribosomes) plus added factors such as tRNAs, amino acids, creatine phosphate, and creatine phosphokinase, giving a solution that will allow the translation of added mRNA molecules. Cell extracts from rabbit reticulocytes or wheat germ are most commonly used. *See also* In vitro protein synthesis.

Cell hybrids: A population of cells produced by the fusion of two different cell lines. *See also* Hybridoma cell.

Cell line: *See* Secondary cell cultures.

Cell immobilization: The conversion of cells from the free mobile state to the immobilized state, either by attachment to a solid support or by entrapment in an appropriate matrix. The three major methods of cell immobilization are: *aggregation* (e.g., by cross-linking with glutaraldehyde); *adsorption* (carrier binding) onto materials such as glass, plastic, brick, or ion-exchange materials; and *entrapment* in gels made from materials such as polyacrylamide, calcium alginate, or κ-carrageenan. The supports can exist in a range of shapes and sizes, including sheets, tubes, fibers, cylinders, and spheres. Whole cells are increasingly used as biocatalysts because they avoid the need for expensive and lengthy extraction and purification of the enzyme(s) of interest. The use of immobilized cells, rather than free cells, allows reuse or continuous use of the biocatalyst. If free cells are used, their recovery and reuse is not feasible because of the expense involved, and they contaminate the product or the waste-stream. Immobilization of cells does not necessarily require the retention of cell viability, as long as the enzyme of interest remains active. Although generally used to catalyze single-enzyme reactions, immobilized cells can be used to catalyze multienzyme reactions. The

most successful use of immobilized cells to date has been in providing glucose isomerase for the production of high-fructose syrups. For example, ruptured *Bacillus coagulans* cells aggregated by cross-linking with glutaraldehyde have been used, as have *Actinoplanes missouriensis* cells entrapped in gelatin cross-linked by using glutaraldehyde and then granulated.

Cellobiase: An enzyme that hydrolyzes cellobiose to glucose. *See also* Cellulase.

Cellobiose: A disaccharide comprising two β-(1,4)-linked glucose molecules, produced by the hydrolysis of cellulose. Cellobiose is the basic structural unit of cellulose, but only exists free in nature in trace concentrations. *See also* Cellulase.

Cell recycle reactor: A reactor (fermentor) where cells are removed from the product and recycled to the tank. Used in particular for recycling activated sludge in wastewater treatment.

Cell sorter: A device designed to separate and analyze individual classes of cells, microorganisms, or organelles from a mixed population. *See also* Flow cytometry.

Cellulase: An inducible enzyme system that degrades cellulose to glucose. Cellulase is present in the digestive juices of snails and wood-boring insects. Cellulase-producing microorganisms in the stomach allow ruminants to partially digest cellulose-containing material such as straw. Commercially used cellulases are produced by strains of *Aspergillus niger, Trichoderma reesei, Penicillium funiculosum,* and *Rhizopus* spp. Three main types of cellulase enzymes are produced by fungi: an *endo*-glucanase that cleaves cellulose randomly; *exo*-1,4-glucanases that produce cellobiose; and cellobiase (β-glucosidase) that breaks down cellobiose to glucose. Cellulase has considerable potential for the large-scale production of glucose and alcohol from cellulose, once the problems of releasing cellulose from its protected environment in lignocellulose have been solved (*see* Lignin). Cellulases are currently used in cereal processing to speed up mash filtration and to increase extract yield; in brewing as a supplement to starch-degrading enzymes to increase the yield of alcohol by degrading cellobiose to a fermentable product; in fruit processing to speed up color extraction from the skins of fruits and to increase liquefaction or maceration of fruits (and vegetables); in waste treatment to speed up the process by causing the release of fermentable sugars; and in the recovery of alginate from seaweed.

Cellulose: The major polysaccharide of plants. It has a structural rather than nutritional role. Cellulose comprises linear polymers of β-1,4-linked D-glucose units. Cellulose has considerable potential for the large-scale production of glucose and alcohol, but this potential has yet to be realized because most cellulose is found as lignocellulose and is thus resistant to enzymic or microbial attack (*see* Lignin). However, the degradation of cellulose by cellulase is used in a number of industrial processes (*see* Cellulase). Beaded cellulose can be prepared by solidification of liquid particles and is used as a support matrix for affinity and ion-exchange chromatography.

Cellulose ion exchanger: A beaded form of cellulose that has been derivatized to form an ionic grouping at the surface. Both cationic forms (containing carboxymethyl groups) and anionic forms (with diethylaminoethyl substituents) are commercially available.

Centrifuge: A mechanical device that may be used in downstream processing as a means of separating systems according to their specific gravity. It operates on the principle that the contents of a rotating container exert a centrifugal force toward the vertical walls of the cylinder. This force causes rapid sedimentation of heavy solid particles through a layer of liquid or of a heavier liquid through a less dense liquid. The centrifugal force is many times greater than gravity and thus allows the rapid separation of solids and liquids with very small density differences. Samples may be placed in discrete tubes attached to the rotor or, in the case of continuous centrifuge, the feed flows through a rotating cylinder or a series of concentric plates. Many different sizes and designs are available to separate either solids and liquids or two immiscible liquids, with and without the presence of solids. The choice depends on the requirements of the process. *See also* Basket centrifuge, Disk centrifuge, Multichamber centrifuge, Scroll screen centrifuge, Tubular bowl centrifuge, Ultracentrifuge.

Centrifugal concentrator (Vacuum centrifuge): A centrifuge in which samples in solution can be placed under a vacuum and dried down. Samples are centrifuged prior to, and during, evacuation to prevent bumping (i.e., samples jumping out of the tube during rapid degassing). The centrifuge bowl can also be heated. This prevents freezing of the sample and increases the rate of evaporation. A bench-scale centrifuge.

Centrifugal contactor: *See* Alfa Laval contactor, Podbielniak extractor.

Centrifugal evaporator: A mechanical device for the large-scale concentration of solutions. It usually consists of a rotating disk or cone heated on one side, with the feed solution fed to the axis of the disk or cone on the other side. The condenser is placed close to this rotor so that the evolved vapor is withdrawn rapidly from the system. Costs are high and the capacity low, making this device suitable only for high-value products.

Cephalosporins: A group of closely related β-lactam antibiotics (i.e., they contain the β-lactam ring common to penicillins) isolated from the mold *cephalosporium*. Although they have a core structure in common with penicillins, they are sufficiently different to be used with patients who are allergic to penicillin.

Chain termination method: A DNA sequencing method. *See also* Dideoxy sequencing.

Chaotropic ions: Ions that disrupt the water structure. Because they reduce hydrophobic interactions, they can be used as desorbing agents for affinity chromatography. Ions can be arranged in order of increasing chaotropicity (e.g., $Cl^- < I^- < ClO_4^- < SCN^- < CCl_3COO^-$).

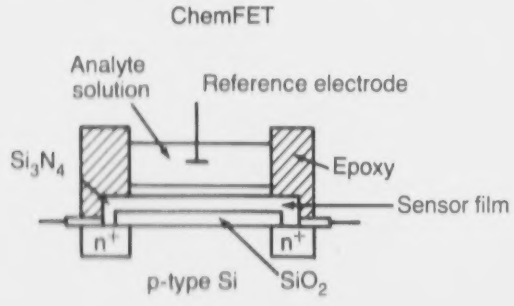
Charon vector: A cloning vector constructed from λ phage. A range of Charon vectors have been constructed, most of which are replacement vectors.

Cheese: Foodstuff produced from milk. The basic process involves the inoculation of milk with lactic acid, producing bacteria (normally *Streptococcus* or *Lactobacillus* spp.) The milk is curdled by the addition of rennet, and the curd is separated from the liquid (whey). The resulting curd is incubated, pressed, and left to ripen. *See also* Rennin, Rennet, Curd, Secondary fermentations.

Chelation: The process by which a molecule (ligand) is attached to a metal ion by two or more donor atoms to provide a chelate ring. The name is derived from *Chelos* (Greek), meaning crab's claw.

Chelating agent: A chemical capable of bonding via two or more donor atoms to a metal ion (e.g., glycine, H_2NCH_2COOH, which can donate via both the nitrogen and one of the oxygen atoms; also EDTA, which has the possibility of six donor atoms). Chelating agents may be used to solubilize and stabilize metal ions in, for example, the preparation of culture media.

ChemFET (chemical field effect transistor): A field effect transistor that has been modified by the deposition onto the gate sites of chemicals that can respond reversibly to changes in the activity of ions in solution. Thus ChemFETs act as sensors, with the advantage of very small size and the ability to react to changes in activity of a number of ions, as each gate can be made to respond to a different ion. However, currently they suffer from lack of reliability and reproducibility. Also called ISFET (ion-selective field effect transistor).



Chemical fusogen: Any chemical that can be used to fuse together two cells or protoplasts. For example, a suspension of plant protoplasts in sodium nitrate solution induces rapid fusion. Polyethylene glycol (PEG) is used to fuse both protoplasts and animal cells (e.g., in hybridoma formation).

Chemical ionization (CI): A method of producing ions for analysis by mass spectrophotometry. It involves a reaction between molecules of the sample and ions produced in a reagent gas by electron-impact ionization in the source. Sample molecules are in much lower concentration than the reagent gas, and a number of different ion–molecule reactions are possible. CI is a much gentler process than electron impact. As a result, the fragmentation patterns are intermediate between very simple field ionization spectra and complex electron-impact spectra. The choice of reagent gas depends on the type of system to be studied. Thus, ammonia is useful for polyhydroxy compounds like sugars; isobutane when the molecular mass is required; and deuterium oxide for active hydrogens. *See also* Fast atom bombardment.

Chemical oxygen demand (COD): A measure of the amount of oxygen required (mg dm^{-3}) for the oxidation of organic matter in water with a strong oxidizing agent at a raised temperature. Samples are treated

with a known amount of boiling acidic potassium dichromate solution for 2.5–4 h. The organic matter is estimated as proportional to the potassium dichromate used. Such correlations are dependent on both the nature and the strength of the effluent. Most organic compounds are oxidized to completion by the dichromate, but benzene, toluene, and pyridine are not oxidized at all. Certain inorganic sulfur-containing compounds, nitrites, and ferrous ions are also oxidized by the treatment, and chlorides may interfere with the reaction. When sewage effluents are tested for COD and biological oxygen demand (BOD), the BOD:COD ratios are normally between 0.2:1 and 0.5:1. *See also* Biological oxygen demand.

Chemisorption: The adsorption of a substance at a surface, involving the formation of chemical bonds between the adsorbate and the adsorbing surface.

Chemoautotroph: An autotroph that synthesizes biological molecules from carbon dioxide and derives its energy by the oxidation of reduced forms of various elements present in the biosphere, such as NH_3 and NO_2^-.

Chemolithotroph: An organism that can obtain its energy from the oxidation of inorganic compounds, such as hydrogen, reduced-sulfur compounds, nitrite, and iron(II). Also called lithotroph.

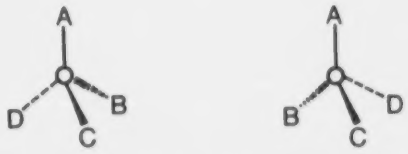
Chemostat: A continuous-culture system in which the growth rate of the culture is controlled by the availability of one limiting component in the medium. *See also* Continuous culture.

Chill haze: A precipitation of protein (probably in association with other compounds, such as tannins and polysaccharides) formed during the cold storage of beer. This problem is overcome in the brewing industry by the use of proteases, such as papain and bromelain, to degrade and solubilize the protein component of the haze. This enzymatic treatment is known as chillproofing.

Chillproofing: *See* Chill haze.

Chimera: Any recombinant DNA molecule produced by joining fragments of DNA from more than one organism (e.g., a bacterial plasmid containing an inserted eukaryotic gene). Named after the mythological beast.

Chirality: Nonidentity of a molecule with its mirror image (i.e., left- and right-handedness). This property, often found in carbon compounds, is demonstrated by the ability in solution to rotate the plane of polarized light to the left or right. These compounds are said to display optical activity. A carbon atom that is attached to four different atoms (groups) is commonly termed a chiral atom, but more strictly the term chiral refers to the environment in which the atom is found (i.e., a chiral center). *See also* Dextrorotatory, Levorotatory.



Chloramphenicol amplification: *See* Amplification of plasmids.

Chloroplasts: Cytoplasmic organelles, found in plants and algae; where photosynthesis takes place.

Chromatin: A term used to describe the complex of DNA and protein found in the eukaryotic cell nucleus. *See also* Chromosome.

Chromatography: A technique used both analytically and in downstream processing for the separation of mixtures of substances based on their ability to partition between a liquid (mobile) and solid (fixed) phase. The technique includes methods that may be subdivided according to the physical nature of the solid support (e.g., gel, paper, thin-layer) and the type of mobile phase (e.g., gas, liquid, supercritical fluid). *See also* Affinity chromatography, Continuous chromatography, Crossflow chromatography, Dye–ligand chromatography, Gas chromatography, Gel filtration, Hydrophobic chromatography, Ion-exchange chromatography, Ion-exclusion chromatography, Partition chromatography, Supercritical fluid chromatography.

Chromatophore: An atom or group of atoms that conveys a particular spectral band (color) to a substance.

Chromogenic substrate: Any enzyme substrate that is converted to a colored product by the enzyme. For example, alkaline phosphatase converts colorless *p*-nitrophenol phosphate to colored (yellow) *p*-nitrophenol. Chromogenic substrates are used to detect enzyme-linked antibodies in techniques such as ELISA and immunoblotting. *See also* Enzyme-linked immunosorbent assay, Immunoblotting.

Chromosome: A highly condensed form of chromatin identifiable in the eukaryotic cell nucleus at the time of cell division.

Chromosome walking: A method for positioning a series of overlapping restriction fragments. It involves the sequential isolation of clones carrying overlapping sequences of DNA. The technique is used mainly to determine the position of a gene on a larger DNA molecule (e.g., a chromosome).

Chymosin: *See* Rennin.

Cibacron Blue 3G-A: A triazine dye used in dye–ligand chromatography for the purification of proteins. (*See* Dye–ligand chromatography). It has been designated the Color Index (C.I.) number 61211. Also known as Cibacron Blue F3G-A, Reactive Blue 2, and Procion Blue H-B.

Cibacron Blue F3G-A: *See* Cibacron Blue 3G-A.

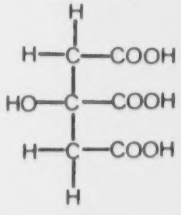
2-μm Circle: A 6-kbp plasmid found in the yeast *Saccharomyces cerevisiae*. It is used as a cloning vector and exists in the yeast cell at a copy number of between 50 and 200. The plasmid contains the gene *leu* 2, which codes for one of the enzymes involved in the conversion of pyruvic acid to leucine. If a *leu* 2$^-$ host is used, transformants can be identified by their ability to grow in the absence of leucine. *See also* Complementation.

***cis* Isomers**: A term used to denote a particular configuration of geometric isomers, where two particular atoms or groups are on the same side of the molecule or atom. Converse of *trans*.

Cistron: A region of DNA that codes for a particular polypeptide.

Citric acid: An industrially useful organic acid. It has been traditionally produced by submerged fungal fermentation of carbohydrate sources such as molasses and glucose hydrolysate. *Aspergillus niger* is the fungus predominantly used, although more recently developed processes preferentially use yeasts. It is also produced by solid-state fermentation, by the traditional Koji process. Citric acid has extensive use in the food, confectionary, and beverage industries as an acidulant. Esters are used in the plastics industry.

Citric acid



C_L: A term used for the concentration (mmol dm^{-3}) of dissolved oxygen in a fermentation broth.

Cladosporium resinae: A fungus commonly found as a contaminant in aviation and diesel fuels. Such fuels invariably contain a small amount of water from seepage during storage. The fungus grows at the fuel–water interface. If unchecked, the fungus can spread into the fuel supply system and cause blockage of filters and fuel lines. This is a particular problem in airplane jet engines and ship diesel engines.

Clarification: A process by which suspended matter is removed from solutions. Several techniques are available, including filtration, centrifugation, and sedimentation.

Clarifier: A large tank with continuous feed and outlet, in which suspended matter is allowed to settle under gravity. The term may also be used to describe liquid–solid centrifuges. *See also* Thickening.

Clavulanic acid: A β-lactam antibiotic produced by *Streptomyces clavuligerus* and a few other *Streptomyces* species. Of particular interest because it is a potent inhibitor of bacterial β-lactamases. It is available, together with the antibiotic, amoxycillin, as a commercial preparation. Clavulanic acid is included to inhibit the degradation of amoxycillin by β-lactamases produced from penicillin-resistant strains.

Cleared lysate: A cell extract that has been centrifuged to remove cell debris, subcellular particles, and most chromosomal DNA.

Clonal propagation: The generation of large numbers of identical plants from a single plant cell or protoplast, or by the growth of plant cuttings. *See also* Clone.

Clone: A group of organisms or cells, all derived asexually from a single ancestral organism or cell, and therefore genetically identical. However, a somewhat looser interpretation of the word "clone" must be used when considering the clonal propagation of plants. Current techniques for plant single-cell and protoplast culture enable thousands of plants to be ultimately derived from a single cell. These plant products should, by definition, each be considered a single clone. However, the product of callus and cell-suspension cultures consists of many abnormal genotypes (somatic variants), so 100% true-to-type clonal propagation does not actually occur.

Cloning: *See* Gene cloning.

Cloning vector: *See* Vector.

Cloning vehicle: *See* Vector.

Clonogenic: A cell capable of generating a clone of cells.

Clostridium: A genus of Gram-positive endospore-forming rod-shaped bacteria. Most strains are strictly anaerobic and obtain energy from fermentation of sugars, starch, pectin, cellulose, amino acids, purines, and other organic compounds. The main habitat of clostridia is the soil. Some are found in the mammalian intestinal tract. A few can cause human diseases by toxin production: botulism is caused by *C. botulinum*, tetanus by *C. tetani*, and gas gangrene by *C. perfringens* and other species. *See also* Acetone–butanol fermentation.

CMC: *See* Critical micelle concentration. Also an abbreviation used for carboxymethyl cellulose.

CoA (CoASH): *See* Coenzyme A.

Coacervation: Separation of lyophilic colloids into two immiscible phases, each of which has a different concentration of the dispersed phase.

Cocurrent flow: A type of flow configuration in continuous processing whereby two process streams flowing in the same direction are brought into contact for the purpose of carrying out heat or mass transfer. This particular configuration is inefficient because once equilibrium between the phases has been reached, no further transfer will occur. *See also* Crosscurrent flow, Countercurrent flow.

Codeine: An alkaloid plant product from *Papaver somniferum*, used as an analgesic.

Codon: Three adjacent nucleotides that code for an amino acid.

Coenocytic: Describes a fungal hypha that has no cross walls (septa) and in which the nuclei are distributed fairly uniformly throughout the cytoplasm. Characteristic of the majority of the Mastigomycotina and Zygomycotina.

Coenzyme: *See* Cofactor.

Coenzyme A: Also CoA or CoASH. A molecule that functions as a

carrier of acyl groups. It is formed by the linkage of adenosine diphosphate via the 5′-phosphate to the phosphate of pantetheine 4′-phosphate. Since the thiol (–SH) group of pantetheine phosphate is responsible for the biological activity of CoA, uncombined CoA is often represented as CoASH. CoA functions as a carrier of acyl groups by forming thioesters (CoASCOR) and provides this C_2 fragment for a range of biosynthetic steps.

Cofactor (coenzyme): A small, nonprotein organic molecule that associates with the protein portion (apoenzyme) of an enzyme and is essential for enzyme function. The complete enzyme (apoenzyme and cofactor–coenzyme) is called a holoenzyme. In the course of the catalytic reaction the coenzyme may be changed chemically and dissociate from the apoenzyme, but it is regenerated in associated reactions and can combine again with the apoenzyme. Examples of coenzymes include NAD^+, $NADP^+$, coenzyme A, and FAD. *See also* Cofactor recycling.

Cofactor recycling: About a third of the known enzymes require coenzyme A, NAD, NADP, FAD, or ATP as a cofactor. For any of these enzymes to be commercially useful, methods must be available for the regeneration of these cofactors after their oxidation or reduction during the catalytic process. Regeneration is part of the normal integrated metabolism of the cell. However, when isolated enzymes and disrupted cells are used, cofactor regeneration is a major problem because cofactors are too expensive to supply continuously. Methods must be developed to regenerate the cofactors in vitro. Methods that have potential are the enzymatic regeneration of cofactors by other enzymes that use cheap substrates and the electrochemical oxidation–reduction of reduced–oxidized cofactors.

Cohesive ends: *See* Sticky ends.

Co-immobilized enzymes: Usually only a single enzyme is immobilized to catalyze a specific reaction (*see* Enzyme immobilization). However, it can be advantageous to immobilize two complementary enzymes. For example, glucose oxidase can be co-immobilized with catalase when hydrogen peroxide produced by glucose oxidase has been degraded by catalase before it can inactivate the glucose oxidase. Other potentially useful co-immobilizations include glucoamylase and glucose isomerase for use in the formation of high-fructose syrups from dextrin.

Col plasmids: Plasmids that code for the antibiotic proteins called colicins.

Cold sterilization: Sterility achieved by ionizing radiation. *Compare with* Autoclave.

Colicins: Antibiotic proteins produced by bacteria carrying col plasmids. Colicins kill bacteria by a range of mechanisms, including the inhibition of active transport, inhibition of protein synthesis, and promotion of DNA degradation. Bacteria carrying col plasmids are obviously immune to the effects of the colicin specified by the col plasmid they are carrying, and this immunity forms the basis of a selection system for cells transformed by col plasmids.

Coliform: A group of bacteria, primarily strains of the genera *Escherichia, Citrobacter, Klebsiella,* and *Enterobacter,* most frequently used as indicators of fecal pollution in assessment of water quality. In the United States, coliforms are defined as aerobic and facultatively anaerobic, Gram-negative, non-spore-forming rod-shaped bacteria that ferment lactose with gas formation within 48 h at 35 °C. In Great Britain, coliforms are defined as Gram-negative, non-spore-forming, oxidase-negative rod-shaped bacteria that can grow aerobically on agar media containing bile salts and ferment lactose with the production of both acid and gas within 48 h at 37 °C.

Colloid: A stable suspension of microscopic particles, size range 1 nm to 1 μm, dispersed in a continuous medium. Two types of colloid may be formed. In *hydrophilic* colloids, the substance consists of macromolecules whose size is in the colloid range. Therefore they exhibit properties characteristic of dispersed systems, such as light scattering, but are soluble in water. These colloids (e.g., gelatin, starch) are thermodynamically stable and are kept in the disperse state by their affinity for water. They can be precipitated only by removal of the water. *Hydrophobic* colloids consist of insoluble particles in a finely divided state suspended in water. These are thermodynamically unstable, but often have a kinetic stability as a result of surface-charge repulsion among the particles.

Colloid mill: A device for grinding matter into microscopic particles such that, on suspension in a liquid, a colloid is formed.

Colony: A group of cells produced from an individual cell when grown on a solid medium such as an agar plate.

Colony hybridization (Grunstein–Hogness method): A method for identifying a clone or clones containing a particular DNA sequence. The colonies are partially transferred to a nitrocellulose membrane

by briefly placing the membrane, with light pressure, on the surface of the nutrient plate containing the organisms. The membrane is then treated to lyse the cells and denature the DNA so that the hydrogen bonds between the DNA strands are broken. Baking them fixes the single-strand DNA to the membrane. The membrane is then washed in a solution containing a radiolabeled DNA probe for the sequence of interest; then the filter is washed and autoradiographed. The position where the probe has bound to the DNA (by complementary base-pairing) is detected as a darkening of the film. This position can then be related to the original nutrient plate and the required clone can be identified.

Column reactor–extractor: A general name given to equipment where the main feature is a long vertical cylinder that may be fitted with devices to promote mixing or coalescence. The simplest design is the spray column, in which one reactant is distributed as a fine spray into the other without any additional means of mixing. Because this is not very efficient, mixing devices are often fitted to the equipment. These can be turbines mounted on a vertical shaft or rotating disks, both of which may also employ a pack of coalescent material between the mixing devices to aid reaction efficiency. *See also* Rotating disk contactor, Oldshue–Rushton contactor, Scheibel contactor, Perforated plate column, Pulsed plate column.

Column volume: *See* Bed volume.

Combined electrode: An electrochemical device that consists of a glass electrode, or ion-selective electrode, and a reference electrode in a single assembly. This design avoids the need for a separate reference electrode.

Comminution: The process of size reduction of materials by crushing and grinding.

Compatibility: The ability of two or more different types of plasmid to coexist in the same cell. Several different types of plasmids can be found in a single cell at any one time. If two plasmids are incompatible, then one or the other is rapidly lost from the cell. Plasmids can be categorized in different *incompatibility groups* on the basis of whether or not they can coexist.

Competent: Adjective describing bacteria that have been treated to enhance their ability to take up DNA molecules. For example, *Escherichia coli* cells are treated with $CaCl_2$ to make them competent prior to uptake of plasmid DNA in transformation experiments.

Competitive inhibitor: Any substance that inhibits an enzyme reaction by complexing with the enzyme at the active site.

Complement: A group of nine serum proteins essential for antibody-mediated immune hemolysis.

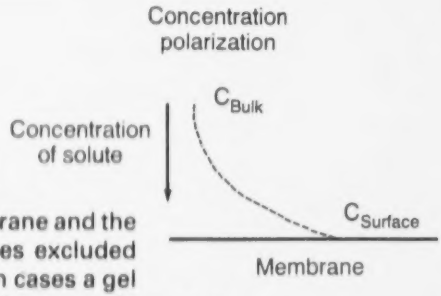
Complementary base-pairing: The ability of two polynucleotide sequences (DNA or RNA) to form a double-stranded structure by hydrogen bonding between bases in the two sequences. The two sequences may be on different strands (e.g., double-stranded DNA) or the same strand (e.g., transfer RNA).

Complementary DNA (cDNA): DNA synthesized from an mRNA template with the enzyme reverse transcriptase. The RNA specifies the base sequence of the DNA by complementary base-pairing. Once the cDNA strand has been synthesized, the RNA chain in this hybrid molecule can be degraded by mild alkali treatment. The single-stranded cDNA can then be converted into double-stranded cDNA by using the Klenow fragment of DNA polymerase I. The resultant DNA fragment can be ligated into a vector and cloned.

Complementation: A method used to identify transformants, where one of the incoming genes complements a defective copy of the same gene on the chromosome of the recipient. For example, the *lacz'* gene (coding for β-galactosidase) will complement a *lacz*-deficient host to give transformants that produce β-galactosidase. These transformants are selected by their ability to produce red colonies on MacConkey's agar.

Concanavalin A (con A): A lectin isolated from the plant *Canavalia ensiformis* (Jack Bean). Concanavalin A binds specifically to residues of α-D-mannopyranose and α-D-glucopyranose with unmodified hydroxyl groups at C-3, C-4, and C-6. Concanavalin A is used to purify glycoproteins by affinity chromatography and to agglutinate cells by cross-linking cell-surface glycoproteins. The protein also stimulates resting lymphocytes to undergo mitosis and multiply (i.e., it is mitogenic). *See also* Lectins.

Concatamer: A series of identical DNA molecules linked in tandem.



Concentration polarization: The increase in concentration of a solute that arises in a fluid boundary layer adjacent to a membrane surface. This increase in solute concentration affects the flux across the membrane and the rejection coefficient of particles excluded from the membrane. In certain cases a gel layer is built up at the membrane surface as a result of concentration polarization. An example is found in desalination, where the transport of water creates a salt build-up close to the membrane surface.

Concentric draft tube fermentor: *See* Airlift fermentor.

Conductimetric sensor: A sensor with a transducer system that measures localized conductivity changes, produced in the proximity of a membrane-linked enzyme by the presence of enzyme substrate. Conductivity changes are proportional to substrate concentrations.

Conidiophore: A specialized fungal hypha bearing conidia(-ium) either at the tip or, rarely, along its length.

Conidium: A spore formed asexually on a fungal hypha, normally at the tip or, more rarely, along its length.

Conjugation: The process whereby genetic information is transferred from one bacterial cell to another by cell-to-cell contact.

Consensus sequence: In cases where there are a number of minor variations between nucleotide sequences that have the same function (e.g., promoters), the consensus sequence gives the most common nucleotide at each position.

Consortia: Groups of microorganisms that coexist or interact when growing together (e.g., in microbial leaching).

Constant boiling mixture: *See* Azeotropic mixture.

Constitutive: Referring to the continuous expression of a gene. Such genes are continuously expressed, being neither inducible nor re-

pressible. Many of the "housekeeping" genes, such as those for the enzymes involved in the Krebs cycle, are constitutive.

Contact angle: The angle between a solid and fluid interface used to determine interfacial tension. It may also be used to assess the surface properties of cells (e.g., bacteria, blood cells).

Contact inhibition: The phenomenon whereby healthy eukaryotic cells growing in culture stop dividing and become immobilized once they have formed a contiguous monolayer covering the surface on which they grow.

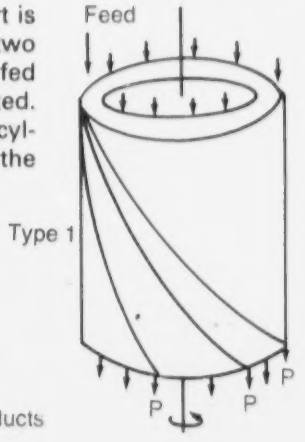
Containment: The prevention of the distribution of an organism, compound, or material that is normally hazardous outside a defined boundary (containment facility). Codes of practice or legislation are often used to restrict the movement and define the zone in which pathogens, biological substances, radioactive compounds, and other hazardous materials can be kept and used.

Containment facility: A building, room, cabinet, or vessel designed to prevent the escape of hazardous organisms or materials. The codes of practice, handling procedures, and containment structure will depend on the potential danger if the material or organism were released or escaped.

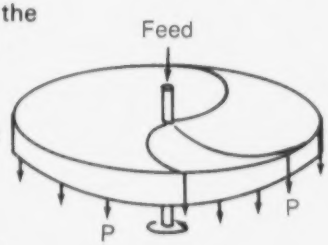
Continuous cell line: *See* Secondary cell cultures.

Continuous chromatography: The operation of chromatographic separations in a continous regime. Several techniques have been devised, and some examples are as follows.

: **(1)**: The chromatographic support is packed into the annular space between two concentric cylinders and the carrier fluid is fed axially while the whole bed is slowly rotated. The feed solution is fed at a point on the cylinder circumference. As the feed rotates, the components in the feed are separated at the base of the cylinder at a series of points, depending upon their individual R_f values.

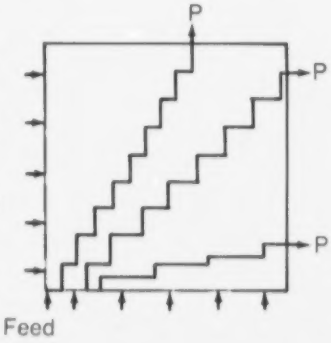


: **(2)**: Another version uses two rotating disks placed close together, with the space filled with the support phase. In this device the carrier fluid and feed material are fed at the center of the disks. Separation results from the rotation of the disks and radial flow of the carrier fluid. Again the separated components emerge at points on the circumference.



Type 2

: **(3)**: Instead of moving the support phase, the direction of flow of the carrier fluid can be varied. Here a rectangular plate is used, with the feed mixture being fed at one corner. The carrier fluid is allowed to flow across the plate in alternate directions at right angles to one another; it carries the separated components up and across the plate in a series of steps.



Type 3

Continuous culture: A system that is used to maintain a cell culture at a steady growth rate. This is normally achieved in a chemostat by pumping medium that contains a growth-limiting substrate into the culture vessel at a constant rate and removing spent medium by an overflow at the same rate. The growth rate of the cells will be controlled by the dilution rate

$$\frac{\text{flow rate of medium}}{\text{vessel volume}}$$

into the vessel. In turbidostat systems, an optical sensor is used to measure the cell concentration in the growth vessel. Signals from this sensor control the rate of addition of fresh medium to the vessel and maintain the cell density within defined limits.

Continuous-flow reactor: Reactors used for the continuous processing of chemical and biological reactions, all possessing the basic facilities for continuous supply of reactants and withdrawal of products. Many different designs have been produced, based on a simple

tank or column with or without facilities for removal of products and recycling of unreacted material. *See also* Stirred-tank reactor, Fluidized-bed reactor, Loop recycle reactor.

Continuous processing: A method of processing whereby raw materials are supplied and products are removed continuously at volumetrically equal rates to maintain the process under the designed operating conditions.

Continuous stirred tank reactor (CSTR): One of the most commonly used reactor designs. Normally an upright baffled cylinder with a vertical rotating shaft, with flat-bladed impellers at regular intervals. The impellers create agitation and mixing within the bioreactor and facilitate aeration. Aeration is achieved by the introduction of air at the base of the vessel via an open pipe or ring sparger.

Controlled-pore glass: Glass beads containing a network of extremely small tunnels and pores (25–70 Å). The pore-size distribution is very narrow, giving the most uniform porosity of any material available. Derivitization of the glass with an alkylsilane provides a suitable support matrix for affinity chromatography.

Convective mass transfer: Mass transfer produced by simultaneous convection and molecular diffusion. The term is used to describe mass transfer between a moving fluid and a boundary surface, which may be a solid or an immiscible liquid.

Convective transfer: Transfer of mass, heat, or momentum in a medium with a nonhomogeneous distribution of concentration, temperature, or velocities. The process is accompanied by a displacement of elements within the system.

Copy number: The number of molecules of an individual plasmid present in a single bacterial cell. Each plasmid has a characteristic value ranging from 1 to 50 or more. Copy number should be considered before a gene is cloned. High copy numbers are an advantage, as this will result in a higher yield of the protein encoded by the plasmid gene, and plasmids with high copy numbers are less likely to be lost from bacterial cultures. However, if the protein product is toxic to the bacterial cell, then a low-copy-number plasmid is to be preferred. *See also* Runaway plasmids.

Corn steep liquor: A component of many fermentation media. It is a byproduct of starch extraction from corn (maize). Although primarily

used as a nitrogen source because of its amino acid content, it also contains vitamins, lactic acid, and small amounts of reducing sugars and polysaccharides.

Corn syrup: A mixture of glucose, sugars, and dextrins; produced by the hydrolysis of starch and often referred to commercially as "glucose", whereas pure glucose is called dextrose.

Cos sites: Name given to the "sticky" or "cohesive" ends found at each end of bacteriophage λ-DNA. They are 12 nucleotides long and are complementary so that they can base-pair with one another. They are produced by restriction endonuclease digestion of λ-DNA, which is initially synthesized as long lengths of repeat units joined together at the cos sites.

Cosmid: A cloning vector that is a hybrid between a phage DNA molecule and a bacterial plasmid. The cos sites of λ-DNA are inserted into a plasmid, to form a molecule that can be packaged (*see* In vitro packaging) into the λ phage head through the presence of the cos sites. These λ phage can then be used to infect bacterial cells. When the cells are plated out, plaques are not formed, because most of the DNA is missing. Transformants can be detected by their ability to grow on a selection medium because of the presence of antibiotic resistance genes encoded on the plasmid. Cosmids can be used to clone fragments of DNA up to about 47 kbp long.

Coulter counter: A device for the automatic counting of cells by measuring the changes in resistance that occur when a suspension of microorganisms in saline solution is drawn through a small glass orifice. A transient increase in resistance occurs when a cell passes through this orifice, the size of which is proportional to the cell volume. The pulses within a defined volume of solution are sorted electronically to give both concentration and size fraction of the microorganisms. Any particles with suitable dimensions may be counted by this device (for example, bacteria, algae, blood cells). Coulter is the name of the manufacturer.

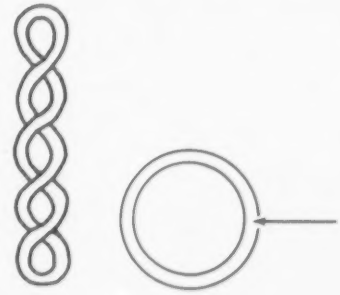
Countercurrent chromatography: This term includes a number of chromatographic methods developed over the past 20 years, with the common feature that a solid support is not used. Two liquid phases of different densities are contained in a coil that slowly rotates about its own axis. This rotation causes the two phases to undergo a countercurrent movement across the original interface, and new interfaces are introduced every half rotation of the coil. Introduction of a solute

into one of the phases allows partition between the two liquids as the segments move through the coil. The two phases are collected at either end of the coil, and the partitioned solute(s) are collected and analyzed. Improved performance can be obtained by reducing the internal diameter of the tubing and the helical diameter of the coil and subjecting the whole system to centrifugal motion. This allows the system to be used in both analytical and preparative modes. Various patterns of centrifugal force fields have been tested; for example, synchronous planetary motion, where the coil rotates about its own axis while revolving about a central axis. This scheme has been shown to produce effective analytical separation, while the toroidal coil planetary arrangement gave efficient preparative separations with, for example, macromolecules and cells in two-phase aqueous partitioning systems.

Countercurrent flow: A type of flow pattern encountered in continuous processing such that one of the process streams is contacted, with the second stream flowing toward (counter to) the first stream. This configuration conveys high efficiency to the resulting process and is commonly found in heat exchangers, where the two streams will normally be separated by glass or metal plates, and in continuous extraction equipment operating in the cascade mode.

Coupling efficiency (immobilized enzymes): *See* Effectiveness factor.

Covalently closed circular (ccc) DNA: A completely double-stranded circular DNA molecule with no nicks or discontinuities (e.g., a plasmid). Most plasmids exist in the cell as *supercoiled* molecules; the ccc DNA folds up in the conformation shown in Figure 1. However, if one of the polynucleotide strands is nicked, the torsional strain is removed and the double helix reverts to the *relaxed* (nonsupercoiled) state referred to as the open circular (oc) DNA (Figure 2).



(1) (2)

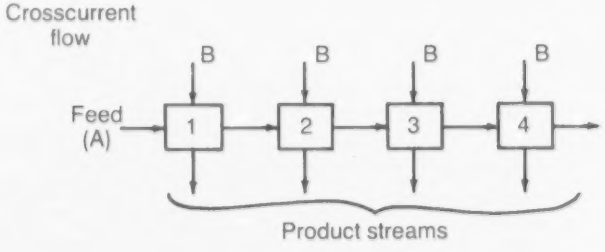
Critical dilution rate (D_{crit}): The lowest dilution rate at which a steady state cannot be attained in a continuous-culture system.

Critical dissolved oxygen concentration (C_{crit}): The concentration of dissolved oxygen in a submerged culture when oxygen becomes the

limiting substrate. Below this value, often in the range 0.1–0.5 ppm, cells may be metabolically disturbed, with subsequent lower yields of biomass or metabolites. Under normal operating conditions the air supply to a fermentor must be adequate to maintain an oxygen concentration well above C_{crit}, especially during conditions of high oxygen demand. Monitoring the dissolved oxygen concentration is achieved with an oxygen electrode.

Critical micelle concentration (cmc): The lowest concentration of a surfactant at which micelles are formed.

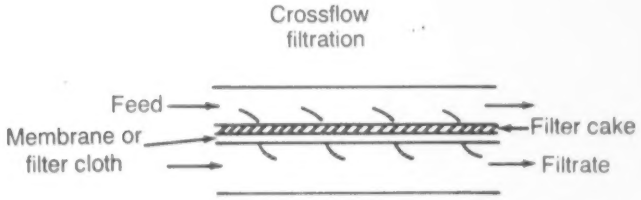
Crosscurrent flow: A type of flow pattern found in continuous processing where the main reactant stream (A) is contacted with a second stream (B) for the purpose of, for example, mass transfer. After this initial contact, feed stream A is brought into contact with another fresh stream B. This succession of contacts with fresh B streams continues until the required process conditions are met in terms of, for example, residual material in stream A. Crosscurrent flow processing gives a number of product streams equal to the number of contacts made, with decreasing concentration of solute as the number of contacts increases. The recovery of the extracted solute then generally requires more concentration than that found for countercurrent flow processing.



Crossflow chromatography: *See* Continuous chromatography.

Crossflow filtration (tangential-flow filtration): An operating regime for a filtering device in which the main fluid flow is parallel to the filter, such that the fluid passes through the filter at right angles to the main flow. This regime minimizes the buildup of filter cake and also the consequential reduction in filtration rate. It allows rapid filtration without the need for filter aids or flocculants. The disadvantage is that a higher pumping energy is required to move the slurry, in

addition to that required for filtration itself. *Compare with* Dead-end filtration.



Crossflow membrane: A membrane used in a crossflow regime, as in crossflow filtration.

Cross hybridization: Hybridization of a DNA probe to an imperfectly matching (less than 100% complementary) DNA molecule.

Crown gall disease: *See Agrobacterium tumefaciens.*

Crud: A solid or semisolid deposit formed at the interface between two immiscible liquids. Also termed insoluble interface.

Cryogen: A substance capable of providing low temperatures, such as a freezing mixture or liquid gases (e.g., nitrogen, air).

Cryogenics: The study of the behavior of matter and materials at low temperatures. The application of low-temperature techniques.

Cryopreservation: Literally, preservation in the frozen state. In practice, this means storage over solid carbon dioxide (−79 °C), in low-temperature deep freezers (−30 °C or less), or in liquid nitrogen (−196 °C). The term is applied to the preservation of cells, protoplasts, tissues, organs, and embryos. At low temperatures, metabolic processes and biological deterioration are minimal, and the preserved material remains genetically stable. Cryopreservation is an ideal way of safely storing important cells such as different strains of microorganisms and hybridoma cell lines. *See also* Cryoprotectants.

Cryoprotectants: Chemicals added to suspensions of cells prior to cryopreservation that enhance the survival of cryopreserved cells. Cryoprotectants bring about changes in cell permeability, freezing point, and response to the stresses of freezing and thawing. Typically, 5–10% w/v or v/v dimethyl sulfoxide (DMSO), glycerol, or sucrose are used.

Cryptic plasmid: A plasmid that does not contain any defined functions other than those required for replication and transfer.

CSTR: *See* Continuous stirred tank reactor.

cp DNA: DNA found in chloroplasts.

ct DNA: DNA found in chloroplasts.

Culture: A population of cells.

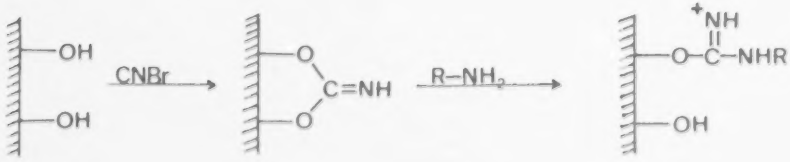
Culture maintenance: Any of the methods used to store or preserve a microorganism with minimum degeneration of its genetic capabilities. This can include subculturing on agar medium, drying, freeze-drying, or cryopreservation.

Curd: A precipitated form of casein produced by the proteolytic action of rennin on milk (curdling). Curd production is encouraged by the presence of bacteria in the milk. Bacteria reduce the pH by lactic acid production to a value close to the pI of casein. The resulting curd is separated from the water component (whey), incubated and pressed, then left to ripen and produce cheese. *See* Rennin, Rennet, Cheese.

Curdlan: A microbial polysaccharide produced by *Alcaligenes faecalis* var. *myxogenes* 10C3. It is an α-1,3-glucan. Heating aqueous solutions of curdlan above 54 °C results in the formation of a nonreversible resilient gel. Curdlan has considerable potential as a gelling agent in cooked foods.

Cyanobacteria: Photosynthetic, oxygen-evolving prokaryotes. Also referred to as blue-green algae, although they are not true algae, which are eukaryotic.

Cyanogen bromide: CNBr. Used in protein chemistry. Generates relatively large peptides from proteins by its ability to cause specific cleavage at methionine residues. However, cleavage is rarely 100% at each residue. Also used to cross-link proteins to various matrices



to form an affinity matrix. Sepharose, agarose, or cellulose can be "CNBr-activated" by the reaction of CNBr with vicinal diols, forming a reactive matrix. This matrix can then be reacted directly with ligands such as proteins or spacer arms containing unprotonated primary amines.

Cybrids: *See* Cell cybrids.

Cyclodextrins: Cyclic compounds composed of six, seven, or eight α-1,4-linked anhydroglucose units: α-, β-, and γ-cyclodextrins, respectively. These compounds are able to form inclusion complexes with a variety of hydrophobic substances, and this property has led to applications in the foods, cosmetics, toiletry, pharmaceutical, and pesticide industries. Cyclodextrins can be produced from starch by the enzyme cyclodextrin glycosyl transferase. An enzyme preparation that produces predominantly β-cyclodextrins has been isolated from a strain of *Bacillus circulans*.

Cytochrome P-450 (also P450, P_{450}): A widely distributed monooxygenase, active in many different biological hydroxylation reactions. The enzyme has considerable potential as a catalyst in the specific hydroxylation of chemicals. The mass production of the enzyme by cloning in yeast is being investigated.

Cytokinins: Plant-growth substances derived from the purine adenine; characterized by their ability to promote cell division and cell and shoot differentiation in cultures of plant cells and tissues. Among the cytokinins commonly used in plant-tissue culture are zeatin, kinetin, benzylaminopurine (BAP), and 2-isopentenyladenine.

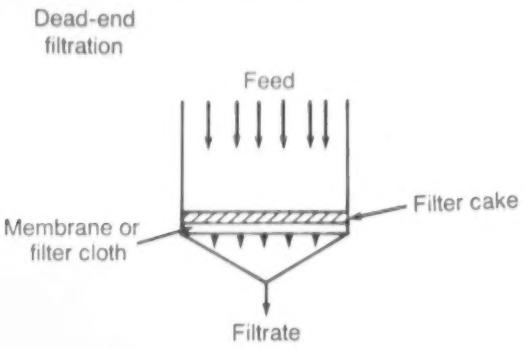
Darcy law (Hagen–Poiseuille): A law concerning the relationship between flux force, V_w, and resistance. The law, applicable to membrane processes, is expressed as:

$$V_w = L_p(\delta P - \sigma/\delta\pi)$$

where σ is the Staverman reflection coefficient with a range from 0 (no solute rejection) to 1 (total rejection of solute); L_p is hydrodynamic permeability; P is the applied pressure; and π is the osmotic pressure.

D_{crit}: *See* Critical dilution rate.

Dead-end filtration: An operating regime for filtration in which the fluid passes perpendicularly to the plane of the filter. This configuration is limited in total throughput as the retained material remains close to the upstream surface of the filter, with consequent decrease in the rate of filtration. *Compare with* Crossflow filtration.



Death phase: The period of time that follows the stationary phase of a microbial culture, when the number of viable cells declines. *See* Stationary phase.

Debranching enzyme (amylo-1,6-glucosidase): An endoglucosidase that hydrolyzes the 1,6-linkages found in polysaccharides such as amylopectin.

Deceleration phase: A period of growth slowdown prior to the stationary phase in a microbial culture. As log phase proceeds in a microbial culture, toxic byproducts tend to accumulate and the substrate (nutrient) becomes increasingly depleted until it is exhausted. Growth of the microorganism therefore slows down and finally ceases, at which point the culture is said to have reached the stationary phase. This period of slowdown in growth is the deceleration phase.

Deep-jet fermentor: A reactor design in which mixing of contents is achieved by the injection of high-pressure air into the bottom of the reactor, or by injection of a recycle stream back into the main reactor under pressure to cause agitation. It is useful for viscous media.

Deep-shaft airlift fermentor: A fermentor design that increases gaseous transfer at high pressures; high levels of dissolved oxygen result. It is used in processes with high oxygen demand, such as the activated-sludge process for waste treatment. The introduction of the fermentor has made the activated-sludge process more economical than the conventional process because it reduces residence time, has

lower running costs, and takes up less space. Incoming waste, returning activated sludge, and compressed air are introduced into the downflow sections of a fermentor shaft. As the mixture rises through the upflow section, the pressure in the system decreases and gas bubbles are released, which increases biomass mixing and aeration.

Defined medium: A medium used for microbial or other cell culture that is of known composition and can be duplicated whenever required. All the components are pure chemicals at defined concentrations. Also called synthetic medium.

Degeneration: The phenomenon whereby a microbial strain decreases in productivity of an excessive metabolite after repeated transfer in culture media. It is essential that an industrial microbial strain should retain the desirable characteristics that led to its selection (e.g., antibiotic potency). The culture should be stored in such a way as to eliminate genetic change, and repeated subculture should be reduced to a minimum. It can be shown that 10–20 serial subcultures may lead to degeneration and a marked loss of antibiotic potency, or to the production of sterile mycelium at the expense of sporing structures.

Degeneration of media: A loss in media nutrient quality during sterilization. This may be caused by interactions between nutrient components of the medium or by degradation of heat-labile components, such as vitamins or amino acids.

Degree of polymerization: A measure of the amount of polymerization of a monomeric compound. It is given as an average number of monomeric units of a molecule in a polymer. The method of averaging must be stated (i.e., number average or weight average).

Deionized water: Water with a very low (zero) content of ionic species, formed by passage down a mixed-bed ion-exchange column, containing both anionic and cationic resins. Water purified by this process may, however, still contain nonionized (i.e., organic) matter. Also called demineralized water.

Del factor: A measure of the fractional reduction in viable organism count produced by a certain heat and time regime during a sterilization process. Thus

$$\text{del factor} = \frac{N_o}{N_f}$$

where N_o is the number of viable organisms present at the start of the sterilization treatment and N_t is the number of viable organisms present after a treatment period t. Also called nabla factor or sterilization criterion.

Delignification: *See* Lignin.

Demineralized water: *See* Deionized water.

Denaturation: **of proteins**: Any treatment that results in the loss of the tertiary (three-dimensional) structure of a protein. Denaturation leads to the loss of biological activity and often results in the precipitation of proteins. Commonly used protein denaturants include urea (8 M), guanidinium chloride (6 M), detergents (e.g., sodium dodecyl sulfate, SDS), heat, and phenol (used to remove protein when preparing DNA or RNA).

: **of DNA**: Any treatment that breaks the hydrogen bonds in a DNA sample, causing the DNA double helix to separate into two distinct strands. This is normally achieved by alkali treatment (*see* Southern blotting) or by heat treatment (*see* Melting of DNA).

Denitrification: Microbial conversion of nitrate to nitrite and nitrogen under anaerobic conditions by strains of a few genera, including *Bacillus* and *Pseudomonas*. This main biological process for the production of N_2 is detrimental in ecosystems. It has been suggested that nitrates can be converted to nitrites by human or animal gut flora. The nitrite that is formed combines with hemoglobin in the blood to form methemoglobin. This can be physiologically dangerous and may cause death. The denitrification of rivers used as a source of drinking water is of considerable interest because of the excess discharge of nitrates into rivers from agricultural fertilizers.

Density-gradient centrifugation: The separation of molecules or particles (e.g., phages or subcellular particles) on the basis of their buoyant density, normally carried out in a gradient of sucrose or cesium chloride. As molecules or particles are centrifuged through an appropriate density gradient, they reach a point where the density of the gradient is equal to their own buoyant density and band at this position. *See also* Ethidium bromide.

Deoxyribonuclease (DNase): *See* Nuclease.

Dermatophyte: A fungus that causes skin diseases.

Desalting: The removal of ionic compounds (salts) from a product solution, often by passage across a membrane (as in reverse osmosis, microfiltration, or dialysis) or by gel filtration.

Detergency: The process by which water-soluble surface-active chemicals are able to wet the surfaces of substances and materials. *See also* Anionic surfactant, Cationic surfactant, Nonionic surfactant.

Deuteromycotina (*Fungi imperfecti*): The group of fungi that includes those that have no sexual sporing stage and reproduce only by means of asexual spores or by fragmentation of mycelium. It includes genera such as *Aspergillus*, *Penicillium*, *Cephalosporium*, *Fusarium*, *Trichoderma*, *Botrytis*, and *Cladosporium*.

Dextran: A branched-chain polymer of glucose residues, linked mainly in 1,6 linkages. Occasionally branches are formed by 1,2, 1,3, or 1,4 linkages, depending on the species from which the polymer is derived. It is produced by a wide range of bacteria, but is obtained commercially by the growth of *Leuconostoc mesenteroides*, with sucrose as a substrate. Dextran is synthesized extracellularly by the enzyme dextransucrase. The molecular weight of the dextran produced depends on the sucrose concentrations of the substrate used. At 70% sucrose concentration, low-molecular-weight (10,000–25,000) dextrans are produced. With low-molecular-weight dextran as a primer and 10% sucrose, high-molecular-weight (50,000–100,000) dextran represents over 56% of the product. High-molecular-weight dextrans are used clinically as plasma substitutes. Cross-linked dextrans are used as gel filtration media and, with functional groups attached, as ion-exchange resins. For these applications raw dextran is purified, partially hydrolyzed, and fractionated by ethanol precipitation to give a product suitable for forming gel filtration media. The soluble polymer chains are cross-linked by glycerin ether bonds by the reaction of dextran with epichlorohydrin in alkali solution to yield a solidified three-dimensional gel (dextran gel). The gels are sold commercially as Sephadex or Sephacryl (Pharmacia). Dextran has also proved useful in forming aqueous two-phase systems with polyethylene glycol. *See also* Dextranase.

Dextran gels: *See* Dextran.

Dextranase: An *endo*-α-1,6-glucanase that hydrolyzes dextran, mainly to isomaltose and isomaltotriose. It is produced commercially from strains of *Penicillium lilacinum* and *Penicillium funiculosum*. Dextrans, produced by *Leuconostoc* sp. in damaged sugar cane and

sugar cane juices, increase viscosity. The viscosity causes problems in clarification and in the evaporation and concentration steps. Addition of dextranase overcomes this problem.

Dextransucrase: *See* Dextran.

Dextrins: Mixture of short-chained polysaccharides formed during the breakdown of starch to maltose and glucose.

Dextrorotatory: Describes the ability of a chiral compound to rotate the plane of polarized light to the right. Often abbreviated as D-, as for example, D-glucose. *See also* Chirality, Levorotatory.

Dextrose: An alternative name for glucose. The term "glucose" is often used commercially to mean corn syrup (a mixture of glucose, sugars, and dextrins produced by starch hydrolysis), and pure glucose is called dextrose.

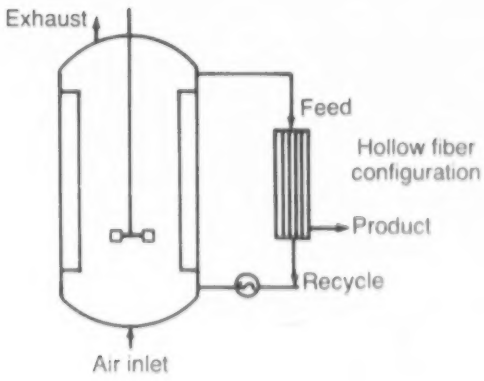
Dextrose equivalent (DE): The DE of a starch hydrolysate is a measure of the extent to which dextrose (glucose) has been produced from starch. The greater the degree of hydrolysis, the higher the DE value. Starch has a DE of 0, whereas complete conversion to dextrose gives a DE of 100. The DE of a solution is determined by measuring the amount of reducing sugars present. *See also* Starch.

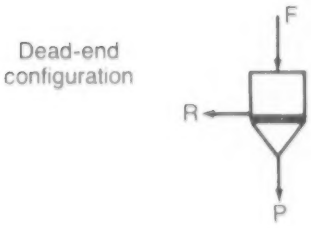
Diafiltration: A process whereby a solution is continuously recycled through a membrane filtration device so that the process stream containing the permeating species is removed. Concurrent with this removal of material, fresh solvent is added to the reactor. Thus within a short time the reactor contents are free of membrane-permeating species.

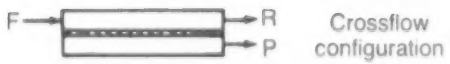
Dialysis: The separation of macromolecules from low-molecular-weight compounds by using a semipermeable membrane. These compounds pass across the membrane into another fluid (water) stream while the macromolecules are retained in the original solution. The process often uses a tubular membrane surrounded by a flowing or stirred stream of pure water to allow rapid diffusion from the membrane surface. It may be defined as the transfer of solute molecules across a membrane by simultaneous diffusion of solvent molecules across the membrane in the opposite direction. *See also* Osmosis.

Dialysis fermentor: A fermentor fitted with a semipermeable membrane that allows the transport of substrate and product across the membrane while retaining the biomass within the reactor.

Dialysis fermentor







Dialyzable: A solute capable of being removed through a semipermeable membrane.

Dialyzate: Fluid flowing through a semipermeable membrane by the process of dialysis.

Diamagnetism: Magnetic behavior of substances that are repelled from areas of high magnetic field. This featuré of all material is clas-

sically explained as a result of the presence of electron pairs in molecules. Diamagnetic materials (e.g., water and most organic compounds) are considered as magnetically unresponsive. Paramagnetic and ferromagnetic effects, if present, normally outweigh the diamagnetic effects. *See also* Magnetic separation techniques, Paramagnetism, Ferromagnetism.

Diatomaceous earth: The skeletal remains of microsopic plants deposited on oceans and lake bottoms 20 million years ago. It is mined from chalklike deposits, ground to a powder, sterilized, and calcined at 800–900 °C. Used as an adsorbant. *See also* Blinding, Kieselguhr, Filter aids.

Dideoxynucleotides: Nucleotides that lack the 3′ hydroxyl group and therefore prevent further chain elongation when incorporated into a growing polynucleotide. *See also* Dideoxy sequencing.

Dideoxy sequencing: A method for sequencing DNA by using dideoxynucleotides. Single-stranded (ss) DNA is required for the method, and is produced by cloning in bacteriophage M13. This ss DNA is used, in four separate experiments, as a primer for the synthesis of the complementary strand of DNA. The process uses the Klenow fragment of DNA polymerase in the presence of low levels of one of the dideoxynucleotides and the four "normal" deoxynucleotides. Complementary strands are produced, varying in length and each ending with a dideoxynucleotide. The strands are analyzed by polyacrylamide gel electrophoresis. Examination of the gel pattern produced allows the DNA sequence to be read directly. Also called chain-termination method.

Dielectrophoresis: A separation technique involving the movement of electrically charged or neutral polarizable particles in a nonuniform electrical field. It has been shown to offer two major advantages. The motion of the particle is toward the region of highest field strength, regardless of electrode polarity. Therefore alternating current may be used, which reduces problems associated with the use of direct current in aqueous solution. The system can be very selective; the force applied to the particles is a function of their polarizability, which is a specific function for nonhomogeneous particles like cells.

Differentiation: A period of cellular development during which cells acquire special characteristics that fit them for the specialized tasks for which they are destined.

Diffuser: A device to facilitate the distribution of one fluid in another to produce a uniform mixture, especially used for gas–liquid mixing.

Diffusion: A process by which molecules or ions mix as a result of thermal motion. The process is dependent on the ease of relative movement of molecules of the components, and thus is most rapid in gases and slowest in solids. Ease of diffusion depends on molecular size. Thus each species can be assigned a molecular diffusivity, which is the rate of diffusion under defined conditions.

Diffusion dialysis: *See* Donnan dialysis.

Diffusion limitation: Factors affecting the diffusion of solvents or solutes. For example, when considering an enzyme immobilized on a solid support, the term relates to factors affecting the diffusion of substrate and products to and from the enzyme. An external diffusion barrier is caused by the thin layer of unstirred solvent that surrounds any particle in a stirred solution (Nernst layer). Second, internal diffusion limitation reflects limitations on free diffusion within the particle matrix caused by the matrix itself.

Diffusivity: The proportionality coefficient of Fick's first law of diffusion, which relates molecular flux and concentration gradient and thus is a measure of the ease of diffusion under defined conditions. *See also* Fick's law of diffusion.

Digoxin: A cardiac glycoside used therapeutically as a heart stimulant, produced from the plant *Digitalis lanata* (foxglove). Also produced by the 12β-hydroxylation of digitoxin, either by suspended cell cultures or by immobilized cells of *Digitalis lanata*.

Dilatant fluid: A fluid for which the viscosity increases as the shear force increases (i.e, the fluid thickens as it is sheared). The behavior of the shear force (τ) with shear rate (γ) follows a power law:

$$\tau = k\gamma^n \qquad \text{where} \quad n > 1$$

See also Pseudoplastic fluid.

Dilution cloning: A method for obtaining clones of cells. Increasingly dilute cell suspensions are plated into wells (often containing non-dividing support cells such as primary cultures of macrophages, which produce mitogenic factors for the added cells). Colonies derived from the most dilute samples are considered to be derived from

a single cell. By repeating the cloning procedure a number of times, true clones can be established.

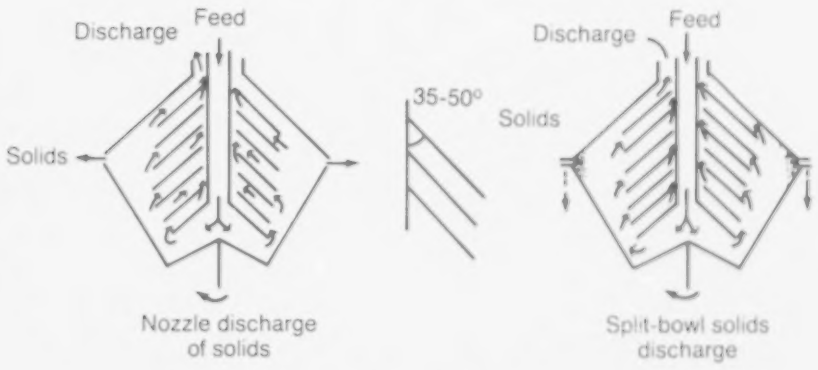
Diosgenin: A steroid plant product isolated from the yam (*Dioscorea deltoidea*) and used in the synthesis of steroids for use as antifertility agents.

Diploid: Cells having chromosomes in pairs.

Direct digital control: Control of a process by computer. This control is achieved when the computer receives information directly from a sensor and, after manipulation of the data via control loops in the computer software, returns a signal to adjust a control device.

Disk centrifuge: Centrifuge commonly used for solution clarification. A typical design consists of a stack of perforated disks (actually truncated cones) spaced 5–12 mm apart, with a half angle of the disk with the vertical of 35–50°. This stack is surrounded by a bowl to contain the solids. The feed enters the bowl near the base and rises up through the stack of disks. The purpose of the disks is to reduce the sedimentation distance, as particles have to travel only a short distance before striking the underside of a disk. Once there, they are removed from the liquid and flow down the disk until they are deposited on the walls of the bowl. Liquid is discharged from the top of the centrifuge via a discharge pipe. Bowl diameter sizes range from 10 to 75 cm, with a centrifugal force of up to 10,000 *g*. Efficiency of separation is about the same as that of a tubular centrifuge, in spite of the lower *g* force. Fluid flows in the range of 20–900 dm^3 per

Disk centrifuge



minute. In addition to their use for solution clarification, they may also be used for liquid–liquid separation and emulsion breaking.

Disk centrifuge with solids discharge: Disk centrifuges that allow the continuous or intermittent discharge of solids from the centrifuge bowl.

: **Nozzle-discharge centrifuge**: In the continuous discharge design, the centrifuge bowl is pierced with a series of nozzles along its periphery. These nozzles are 1–3 mm in diameter and allow the continuous flow of solids as a slurry from the bowl into a surrounding container. The remainder of the construction is similar to a normal disk centrifuge. The equipment can operate on a once-through system with some recycle of solids. It will allow more extensive dewatering of the slurry up to 50% w/w solids, but more typical values are 20–30% w/w.

: **Intermittent-discharge centrifuge**: In this design, openings along the periphery of the bowl are closed by valves that can be opened intermittently. An alternative design allows the centrifuge bowl to form a horizontal slit, through which the solids are discharged. In these designs the solids can be accumulated as a relatively dry cake, so little fluid is lost.

Dispase: A commercially available enzyme preparation used to break down connective tissue and thus release viable cells for cell culture.

Dissolved oxygen concentration: A measure of the dissolved oxygen concentration in a medium (mmol dm^{-3}). It is normally determined in a fermentation broth with sterilizable galvanic or polarographic electrodes.. *See also* Critical dissolved oxygen concentration.

Dissolved oxygen electrode: A device for measuring oxygen in solution. Various types are available, but the majority rely on a sensor consisting of a semipermeable membrane through which oxygen diffuses at a rate proportional to the partial pressure of oxygen outside the membrane. Once inside the sensor, the oxygen is reduced at a cathode to provide a current that is proportional to the partial pressure of oxygen, providing that the oxygen diffusion is the limiting step. *Note*: the partial pressure (or activity) of oxygen is measured, not the concentration. The thin oxygen-permeable membrane protects the electrodes from both chemical and biological contamination. *See also* Phillips and Johnson tube.

Distillation column: A device to facilitate the separation of components as a function of their relative volatilities or boiling points. The device normally consists of a cylindrical column with various forms of packing or coalescence devices to aid the establishment of equilibrium between the vapor and liquid–condensate phases within the column. The complete attainment of equilibrium between these phases is termed a plate. Hence, a measure of plate efficiency can be used to measure the efficiency of a column for a particular separation. The height equivalent to a theoretical plate (HETP) (i.e, the height of a column that would give complete equilibrium) also measures this column efficiency.

Distributed digital control: A process consisting of a number of unit operations is said to be under distributed digital control if each unit operation is individually controlled by its own computer.

Distribution coefficient: The ratio of the total analytical concentration of the substance in one phase to its total analytical concentration in the other. Under defined conditions, the distribution coefficient describes the distribution of a substance between two phases in a heterogeneous system of two (liquid) phases in equilibrium. This description distinguishes the distribution coefficient from the partition coefficient, which requires a single identical form of the solute in the two phases. For example, in an oil–water system, the distribution of a solute *A* between these solvents is defined by:

$$D = \frac{C_A\,(\text{oil})}{C_A\,(\text{water})}$$

Compare with Distribution constant, Partition coefficient.

Distribution constant: The same as distribution coefficient, with concentrations replaced by activities. *Compare with* Distribution coefficient, Partition constant.

λ DNA: A single linear DNA molecule (49 kbp) found in the head of λ bacteriophage. The molecule has sticky ends (cos sites) of 12 nucleotides at each end, which are complementary. This allows the DNA to circularize by complementary base-pairing, which is a necessary prerequisite for replication and for insertion into the bacterial genome when λ phage infects bacteria.

DNA duplex: The normal double-stranded form of DNA.

DNA ligase: An enzyme that has the physiological role of catalyzing the synthesis of a phosphodiester bond between the 3′ hydroxyl group and 5′ phosphoryl group at a single-strand break in double-stranded DNA. Because such nicks are generated in important processes such as DNA replication and DNA repair, DNA ligases are found in all living cells. However, two forms of the enzyme have found particular use in genetic engineering. These are DNA ligase (MW 74,000) from *Escherichia coli*, which is NAD-dependent, and T4 ligase (MW 68,000) from bacteriophage T4, which is ATP-dependent and also requires magnesium ions. Both enzymes are extensively used for covalently joining restriction fragments that have been joined by the base-pairing of their mutually cohesive "sticky ends." The T4 enzyme, purified from T4-infected *E. coli*, is used most because it is easier to prepare. The T4 enzyme also has the additional advantage that at high concentrations it can join DNA fragments that have "blunt ends." In this case the molecules to be joined are not initially held together by hydrogen bonds between mutually cohesive termini (sticky ends). The *E. coli* enzyme cannot achieve this. The T4 enzyme is now prepared by cloning its gene in phage vectors.

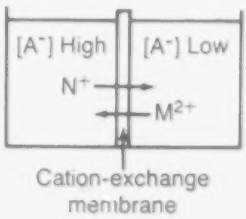
DNA polymerase I (DNA pol. 1): An enzyme isolated from *Escherichia coli*, which synthesizes double-stranded DNA by using single-stranded DNA as a template. A primer is required. The enzyme also contains both 5′ to 3′ and 3′ to 5′ exonucleolytic activities. It is used to radiolabel DNA by nick translation. *See also* Klenow fragment.

DNA polymerases: Enzymes that synthesize a new strand of DNA complementary to an existing DNA or RNA template. *See* Reverse transcriptase, Klenow fragment, DNA polymerase 1, *Micrococcus luteus* polymerase, T4 DNA polymerase.

DNA sequencing: Determination of the order of nucleotides in a DNA sample. *See also* Maxam–Gilbert method, Dideoxy sequencing.

Donnan dialysis: When two solutions of different concentrations are separated by an ion-exchange membrane, then ions of the appropriate sign will migrate across the membrane from the higher concentration to the lower. This migration causes the reverse movement of the other ions to maintain electroneutrality. Migration occurs until the relative concentrations of ions on both sides of the membrane are constant. Also called diffusion dialysis.

Donnan Dialysis



Donnan (membrane) equilibrium: When two solutions, a polyelectrolyte and a salt, are separated by a membrane such that the ions in the salt solution are able to diffuse across the membrane but the polyelectrolyte is contained, then the distribution of ions will be influenced by the presence of the polyelectrolyte. Hence their concentrations will be unequal on both sides of the membrane. This variation of concentration is termed the Donnan equilibrium. In turn, it generates a potential difference across the membrane, the Donnan membrane potential. Also called Gibbs–Donnan.

Donnan (membrane) potential: *See* Donnan equilibrium.

Dot–blot: A method for rapidly screening a large number of DNA or RNA samples to detect and quantify the presence of a particular base sequence. The aqueous samples are applied to a nitrocellulose filter, either by dotting them on with a pipet or by adsorbing them onto the paper by means of suction through a custom-built apparatus. This dot–blot apparatus comprises a series of wells (10 × 10) drilled in a Perspex block. Directly beneath the block is a sheet of nitrocellulose paper, which in turn is connected to a vacuum source. Individual samples are placed in separate wells. When a mild vacuum is applied, the liquid in each well passes through the membrane, leaving the DNA bound as individual dots on the nitrocellulose sheet. The filter is then incubated in a solution containing a radiolabeled probe for the required sequence. It is washed, dried, and then subjected to autoradiography to detect samples that have hybridized to the probe. The extent of blackening of the film can be taken as a semiquantitative measure of the amount of sample present.

Double digestion: The cleavage of a given DNA molecule with two different restriction endonucleases, either consecutively or together.

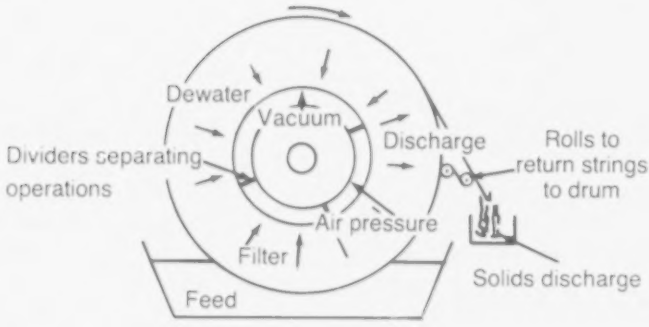
Driselase: A mixture of cellulase and a pectinase derived from a basidiomycete, used to degrade cell walls and produce protoplasts.

Downstream processing: A general term given to the unit operations required to separate, concentrate, and purify a product arising from a reactor–fermentor. The processes that take place at reactor level are termed upstream processing.

Drum filter: A device for filtration that consists of a horizontal drum covered by a cloth (filter cloth). The drum rotates in a bath continuously fed by a process stream. Vacuum applied to the inside of the drum draws the filtrate through the cloth into the drum, from which

it is continuously removed. The filter cake (precipitate) is retained on the cloth, from which it can be removed periodically. Drum filters can be designed to allow the *in situ* washing of the precipitate on the filter, followed by dewatering by increasing the vacuum. Various operating procedures may be employed to maintain the rate of filtration, including the use of a precoat on the filter cloth, to minimize blinding or improve the filterability of slimy precipitates. The filter cake may be removed continuously from the filter by the application of a scraper or knife, which can be set to remove the cake once the desired cake depth has been reached. An alternative is a string discharge, in which a series of endless belts run around the drum and a separate cylinder. These strings continuously lift off the cake as they detach from the drum.

Drum filter



String discharge

Scraper discharge
alternative procedures

Dunaliella bardawil: A unicellular green alga with potential as a source of glycerol. The alga grows in sunlight and in high saline concentrations, accumulating intracellular free glycerol to counterbalance the salt concentration of its external environment. It can produce up to 85% of its dry weight as glycerol.

Dye exclusion tests: Tests used to determine the viability of cells. One drop of stain (e.g., trypan blue) is mixed with one drop of cell suspension. After 5 min the cells are washed with culture medium and observed on a light microscope with white-light illumination. Living cells remain unstained, but dead cells accumulate the stain. *See also* Fluorescein diacetate.

Dye–ligand chromatography: Affinity chromatography using dyes as the affinity ligand. The affinity ligands most widely used for protein purification are the triazine-based reactive textile dyes. These dyes can bind representatives of virtually every protein class. Reactive dyes are polyaromatic molecules that consist of a chromophore (azo phthalocyanin or anthraquinone) linked to a reactive group (usually a mono- or dichlorotriazine ring) and made water soluble by the incorporation of sulfonic or carboxylic acid groups. The procion dyes are among the most common groups used for this purpose.

Ectomycorrhiza: ***See*** Mycorrhiza.

Eddy diffusion: Diffusion that results from eddy formation in a fluid and thus produces more rapid mixing and higher diffusivities. An eddy is a macroscopic element of a fluid possessing rotational movement and is a feature of turbulent flow.

EDTA (ethylenediaminetetraacetic acid): A multidentate chelating agent used extensively as a titrant in analytical chemistry for determination of metals in solution, and as a means of solubilizing metals in the preparation of culture media.

Effectiveness factor: Also referred to as coupling efficiency or activity yield. A term used when immobilizing cells or enzymes. It is the activity of the immobilized enzyme (or cells) divided by the activity of an equivalent quantity of free enzyme (or cells). The activity of an immobilized enzyme is defined as the number of grams of product formed per gram of immobilized enzyme (or cells) per hour, or as the number of grams of product formed per milliliter of reactor volume per unit of time.

Effective kinetics (of an enzyme): *See* Intrinsic kinetics.

Effective yield: The quantity of cells produced from unit weight of substrate in a continuous-culture system.

Effluent: The liquid and solid waste materials of a manufacturing process. Typical wastes can include unconsumed inorganic and organic media components; microbial cells; suspended solids; filter aids; waste wash water from cleansing operations; and water contaminated with solvents, acids, alkalis, and human sewage. Emissions are governed by legislation. *See also* Biochemical oxygen demand, Chemical oxygen demand.

Elasticity: One of the fundamental parameters of rheology. Observed as the energy retained in a fluid such that some flow reversal occurs when shear stress, the force causing fluid flow, is removed.

Electro-blotting: The electrophoretic transfer of separated DNA, RNA, or protein molecules from a gel matrix onto a nitrocellulose sheet, where they bind. *See also* Southern blotting, Protein (western) blotting, Northern blotting.

Electrochemical reactors: Another name for biochemical fuel cells.

Electrochemical sensor: A monitoring device based on the production of a change in an electrical property (such as variation in current, potential, or resistance) proportional to corresponding changes in the analyte concentration.

Electrodialysis: The application of a potential difference across a membrane to facilitate the transport of ions. The membranes contain ion-exchange groups and carry a fixed electrical charge. By suitable choice of the membrane, either cations or anions can be transported. The technique is used for desalting and concentration of proteins from fermentation broths, as well as their fractionation and purification. Other applications include desalting of cheese whey and recovery of reagents used in downstream processing.

Electroendosmosis: The movement of electrophoresis buffer through a supporting medium (e.g., paper, agarose) during electrophoresis. Ideally, all support media used for electrophoresis should have zero charge. In practice, even the best media contain a small number of attached charged groups (e.g., agarose contains sulfate groups). Such charges are balanced by the presence of counterions, and in an electric field these cations and associated water molecules migrate toward the cathode. This solvent flow, termed electroendosmosis, will tend to carry sample molecules with it. Its movement, in the opposite direction to that of most biological molecules, is directly related to the content of ionic groups in the medium.

Electrofusion: The fusing of cells (e.g., in the production of hybridomas) or protoplasts by the use of an electric field. A high-frequency alternating field (≈1 MHz) is applied. This field induces dipoles on the cells, which causes them to align. Cells are then fused by the application of a brief (microsecond) direct-current pulse (≈1000 V/cm). The pulse induces structural and permeability changes in cell membranes (micropore formation), which allows intermixing of the cellular contents and fusion of adjacent cells.

Electropermeabilization: *See* Electroporesis.

Electrophoresis: A separation process whereby charged particles (ions) may be separated by their movement through a stationary fluid or gel under the influence of an electric current. Ions can be separated because the rate of migration depends on size and charge of the ion. Because the extent of dissociation of a substance into ions may be pH-dependent, change of pH can provide an additional means of separation.

Electroporation: *See* Electroporesis.

Electroporesis: Also known as electropermeabilization or electroporation. A general method for introducing large molecules into cells, particularly for transforming cells. Cells or protoplasts in solution are subjected to a brief (≈1 ms) direct-current pulse (≈1000 V/cm), which induces changes in the structure and permeability of the cell or protoplast membrane (formation of micropores). If carried out in the presence of molecules such as DNA, this allows passage of DNA into the cell (transformation).

ELISA: *See* Enzyme-linked immunosorbent assay.

Eluant: A solution used for the elution of species from an adsorbent.

Elution profile: A diagrammatic representation of the amount of substance removed from an adsorbent as a function of volume of eluant passed. Thus the elution of a sequence of substances can be represented by a series of concentration peaks at varying volumes of eluant passed. *See also* Breakthrough profile.

Elution volume: Volume of eluant necessary to remove a particular substance from an adsorbent.

Embryo culture: Plant regeneration by the aseptic culture of a zygote embryo. The embryo is excised from either the seed or ovule and

planted on a nutrient medium. Subsequent embryo development and germination occurs as it would from the seed.

Embryogenesis: A pathway of differentiation in plants, induced in undifferentiated cell, tissue, or organ cultures by appropriate control of nutritional and hormonal conditions, that results in the formation of organized embryolike (embryoid) structures. Under appropriate cultural conditions these organized structures can develop to form plantlets and eventually whole plants.

Emulsion: A colloidal suspension of one liquid in another (e.g., oil and water). According to their relative concentrations, it is possible to form either an oil-in-water or a water-in-oil emulsion. The stability of an emulsion can be increased by the presence of surface-active agents (i.e., surfactants or emulsifiers). Used, for example, in steroid transformations to get the steroid into the correct environment for enzymic reaction.

Emulsifier: A substance that aids the formation and stability of an emulsion; a surfactant.

Enantiomers: Isomers of a molecule that possess an asymmetric atom, such that the arrangement of groups (atoms) about this atom are different, with one isomer the mirror image of the other. *See also* Optical activity, Chirality.

End-filling: The conversion of a DNA fragment with sticky ends to one with blunt ends by the enzymatic synthesis of a strand complementary to the single-strand extension.

Endomycorrhiza: *See* Mycorrhiza.

Endonucleases: Enzymes that cleave phosphodiester bonds within a nucleic acid molecule. *See also* Nuclease, Restriction endonucleases.

Endospore: A bacterial spore formed within the cell of species of *Bacillus, Clostridium, Sporolactobacillus, Desulfotomaculum, Sporosarcina,* and *Thermoactinomyces.* The spores may be extremely resistant to heat, UV, X-rays, or chemical agents. *See also Bacillus, Clostridium.*

Endothermic reaction: A chemical reaction during which energy is adsorbed from the surroundings. Some input of energy to the system is required to achieve reaction. Endothermic reactions therefore have

a positive enthalpy change and cannot occur spontaneously. *Compare with* Exothermic reaction.

Enrichment culture: A technique that leads to an increase in the number of a given organism relative to the numbers of other types of organism in the original inoculum in a liquid medium. The procedure involves taking a mixed culture and providing conditions either suitable for growth of the required organism or unsuitable for growth of the other organisms. This procedure is normally done by the use of particular substrates or the inclusion of specific inhibitors. It may be necessary to subculture a number of times before the required organism can be isolated after streaking onto solid media.

Ensiling: The solid-substrate fermentation of agricultural vegetation, using indigenous microflora. It is carried out for 1–2 weeks at 25–30 °C, during which time *Lactobacillus* spp. become the dominant organisms. Lactic acid is produced, which inhibits the growth of putrefactive bacteria. The absence of oxygen prevents the growth of aerobic mold fungi.

Enterotoxin B: A secreted, single-chain protein (MW 28,400) that is the causative agent of staphylococcal food poisoning. However, the compound is also mitogenic and may have uses in the treatment of cancer and in immunology.

Entrapment: One of the more popular techniques for immobilizing enzymes or cells. The enzyme or cell is entrapped within a polymeric mesh by carrying out the polymerization or cross-linking reaction in the presence of the enzymes or cells in question. Entrapment media that have been successfully used include polyacrylamide gels, calcium alginate gels, agar gels, and κ-carrageenan. The pores of the matrix are large enough to allow substrates, products, and nutrients to diffuse through, but small enough to prevent loss of the higher-molecular-weight biological material. *See also* Microencapsulation, Enzyme immobilization, Cell immobilization.

ENV Glycoproteins: Glycoproteins found in the lipoprotein envelope of RNA tumor viruses (retroviruses). They are necessary for binding the virus to the surface of host cells on infection. ENV is the name given to the gene that codes for the glycoprotein.

Enzyme electrode: The combination of an immobilized enzyme with an ion-selective electrode sensor to provide a selective and sensitive method for detecting a given compound in a complex solution. The

compound to be measured is a substrate of the enzyme. The enzyme is usually immobilized on the ion-selective electrode, either by chemical immobilization or by entrapment in an inert matrix. The substrate to be measured diffuses through an external membrane to the enzyme and is converted to a product that is measured at the surface of the ion-selective electrode. In some designs the change in activity (concentration) of one of the reactants is measured. The detection range of most enzyme electrodes is $10^{-2} - 10^{-4}$ M. One of the first enzyme electrodes to be described was the use of glucose oxidase to measure glucose concentration. In this instance, oxygen uptake was measured with an oxygen electrode.

$$\text{glucose} + O_2 + H_2O \xrightleftharpoons{\text{glucose oxidase}} H_2O_2 + \text{gluconic acid}$$

Over 100 enzyme electrodes have now been described. They can determine a spectrum of compounds, including amino acids, steroids, sugars, alcohols, and inorganic ions. For example, penicillin levels in fermentation broths are routinely determined using a pH probe coated with immobilized penicillinase. The pH electrode detects penicilloic acid produced by the enzyme.

$$\text{penicillin} \xrightarrow{\text{penicillinase}} \text{penicilloic acid}$$

See also Biosensor.

Enzyme engineering: *See* Protein engineering.

Enzyme immobilization: The conversion of enzymes from the free mobile state in solution to the immobilized state. The use of immobilized enzymes, rather than the free enzyme, has particular advantages for industrial processes because it allows the re-use or continuous use of the enzyme, which in many cases may be expensive to produce. Immobilization can also increase the stability of the enzyme. If the enzyme is used in free solution it cannot be recovered and also results in contamination of the product or waste stream. Various methods have been used to immobilize enzymes. These include *entrapment*, either in cross-linked insoluble gels (e.g., acrylamide), within the microcavities of synthetic films, or microencapsulation within a semipermeable polymer membrane; *covalent binding* to an insoluble carrier polymer (e.g., cellulose); *adsorption* onto an insoluble matrix (e.g., polystyrene or glass); and *copolymerization* of the enzyme with a cross-linking agent such as glutaraldehyde, to produce an insoluble matrix of enzyme.

Enzyme-linked immunosorbent assay (ELISA): A highly sensitive assay technique for detection and measurement of antigens or antibodies in solution. Particularly useful in immunodiagnostic applications such as serodiagnosis to detect antigens from a wide range of specific viruses, bacteria, fungi, and parasites, and to measure the presence of antibodies against these various microorganisms. It is also used to monitor factors involved in noninfectious diseases such as hormone levels, hematological factors, serum tumor markers, drug levels, and antibodies, and to measure vaccine responses. The technique is particularly useful for screening hybridoma clones for the production of monoclonal antibodies. The name derives from the fact that the assay uses enzyme-linked antigens or antibodies to amplify an antigen–antibody reaction. A single enzyme-linked antibody–antigen complex can convert orders of magnitude more colorless substrate molecules into detectable colored products, thus considerably amplifying the original antigen–antibody reaction. Also, the antigen or antibody is absorbed onto the surface of the well of a microtiter plate and all the relevant reactions take place in solution inside the well.

Enzyme reactor: *See* Bioreactor.

Epigenetic: Factors that influence the phenotype but do not arise in the genotype.

Epiphase: Term applied to the less-dense phase in a two-phase system, particularly where the two phases may be similar in properties (e.g., two-phase aqueous systems). *Compare with* Hypophase.

Episomes: Plasmids that replicate by inserting themselves into the bacterial chromosome. They are maintained in this form through numerous cell divisions, but at some stage exist as independent elements. Also known as integrative plasmids.

Episomal: Existing as an independent, autonomously replicating, genetic element not associated with cellular chromosomes.

Epitope: The region of an antigen to which the variable region of an antibody binds. Most antigens have a large number of epitopes, and therefore a polyvalent antiserum to the antigen will contain a large number of different antibodies, each antibody capable of binding to a different epitope on the antigen.

Eppendorf: The name of a German manufacturing company. However, the word is used in laboratory jargon to describe small (0.5–1.5 cm^3) plastic centrifuge tubes (Eppendorf tubes) used in microcentrifuges, and to describe disposable plastic tips used on micropipets (Eppendorf tips).

Ergot alkaloids: A group of pharmacologically active compounds, mainly produced by species of *Claviceps* while they are growing as fungal parasites of grasses and cereals. Historically, the alkaloids were obtained by extraction from sclerotia formed on rye infected with the fungi. Now ergot alkaloids are produced by submerged culture of *Claviceps* rather than by the systematic infection of rye. Ergot alkaloids have a wide range of uses, including treatment of postpartum hemorrhage, migraine, orthostatis hypotension, senile cerebral insufficiency, and Parkinson's disease. The biotransformation of simple ergot alkaloids has also been used to generate a further range of ergot alkaloids.

Erythromycins: A number of closely related nonpolyene macrolide antibiotics that are produced by *Streptomyces erythraeus*. Although broad-spectrum, they have strong activity against *Staphylococcus aureus* and *Streptococcus faecalis*, and are mainly used to treat patients sensitive to penicillin. These antibiotics inhibit bacterial protein synthesis.

Escherichia coli: A species of Gram-negative, facultatively anaerobic, rod-shaped bacteria. First isolated as a cause of diarrhea and named by Escherich in 1885. It is normally found in the lower intestinal tract of warm-blooded animals. Many strains may show opportunist pathogenicity. It is used as an indicator organism for fecal contamination of water. It grows readily on simple nutrient media and has been used extensively as a model microorganism in biochemical and genetic investigations. Because a range of vectors may be used to introduce new genetic material into *E. coli*, it has been used extensively in genetic engineering studies. *See also* Coliform.

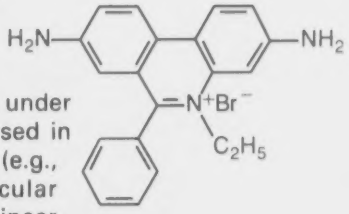
Essential oil: An oil extracted from biological material, such as plants or animals, that possesses some property of the material (e.g., smell or taste). Used in production of perfumes and flavorings (e.g., Jasmine oil, musk oil, peppermint oil).

Established cell line: Any cell line that appears to be capable of unlimited growth through in vitro propagation.

Ethanoic acid: *See* Acetic acid.

Ethanol (ethyl alcohol): C_2H_5OH. An alcohol with a wide range of industrial uses, mainly as a solvent, as a chemical intermediate, and as a fuel (*see* Gasohol). About 40% of the world production of ethanol relies on fermentative processes; the rest is prepared chemically from ethylene gas. Production by fermentation is more prevalent in less industrialized nations. The economic viability of the fermentative production of alcohol depends on the current price of crude oil. Yeasts are the only organisms currently used for large-scale industrial ethanol production. Alcohol is produced by the fermentation of saccharine raw materials such as sugar cane juice, sugar beet juice, molasses, or sweet sorghum. Starchy raw materials such as cereal grains and starch root plants are also used, but cannot be fermented directly by yeast. Such material must first be broken down to fermentable sugars by the use of enzymes or weak acids. These preliminary treatments add about 20% to the cost of the alcohol plant. Alcohol recovery, invariably by distillation, is energy-intensive, accounting for over 50% of the ethanol plant energy consumption.

Ethidium bromide: A planar, polycyclic molecule, used to detect DNA (e.g., in gels) by staining. Ethidium bromide binds to DNA by intercalating between adjacent base pairs and can be identified by its fluorescence under UV light. Ethidium bromide is also used in the separation of supercoiled DNA (e.g., plasmids) from linear and open-circular DNA. Ethidium bromide binding to linear and open-circular DNA causes partial unwinding of the double helix, with a resultant decrease in the buoyant density. Supercoiled DNA, however, can only bind limited amounts of DNA because of its reduced ability to unwind, and therefore its buoyant density is decreased by a much lesser amount. These different forms of DNA can therefore be separated on the basis of their different buoyant densities by density-gradient centrifugation.



Ethylene: A gas, C_2H_4. Particularly important in plant sciences because it functions as a plant-growth substance. It is involved in many auxin-induced growth responses, and it plays a part in leaf aging and the ripening of some fruits, such as tomatoes.

Ethylenediaminetetraacetic acid: *See* EDTA.

Eukaryotic cell: A cell whose genetic material is organized into a well-

defined compartment (the nucleus). Plant and animal cells, fungi, and yeast are all eukaryotic. *Compare with* prokaryotic cell.

Eupergit C: Oxirane acrylic beads obtained by the copolymerization of methacrylamide, methylene bis(methacrylamide glycidyl) methacrylate, and allyl glycidyl ether. Used as a support matrix for affinity chromatography in downstream processing.

European Molecular Biology Laboratory (EMBL) nucleotide sequence data library: A compilation of all published nucleotide sequences. The 1986 issue (release no. 9) contained 7630 entries, with 7,813,214 nucleotides.

Eutrophication: The enrichment of a body of water, for example, by the input of organic material or by surface runoff containing nitrates and phosphate. Eutrophication may occur naturally, but is often caused by pollution or effluent disposal. It leads to an increase in the growth of photosynthetic algae, which results in the depletion of the dissolved oxygen content of the water.

Evaporation: The removal of a liquid by conversion into its vapor by the application of heat or vacuum.

Evaporator: An apparatus designed to carry out evaporation of a liquid. Sometimes operated at a reduced pressure to reduce heating costs. Various designs are available to meet the particular requirements of the process and product, especially product heat stability. *See also* Centrifugal evaporator, Falling-film evaporator, Flash evaporator, Forced-circulation evaporator, Natural-circulation evaporator, Rising-film evaporator, Wiped-film evaporator.

Exchange capacity (ion exchange): The number of ions (generally measured in milliequivalents per gram of dry resin) that can be exchanged by a particular resin. Capacity of a resin depends on the number of exchange sites and therefore on the type of resin. *See also* Gel resin, Macroporous resin.

Exclusion chromatography: *See* Gel filtration.

Exons: Those parts of the sequence of a eukaryotic gene that code for the final protein product. In most eukaryotic genes, noncoding regions known as introns separate the coding region into a number of distinct exons. *See also* Introns.

Exonuclease III: A 3′ to 5′ exonuclease, isolated from *Escherichia coli*, that starts from each 3′ end of a DNA duplex, degrading each 3′ strand, leaving single-stranded 5′ extensions. It is used in conjunction with S_1 nuclease to create deletions in cloned DNA molecules.

Exonucleases: Enzymes that sequentially remove nucleotides from the ends of a nucleic acid molecule. *See also* Nuclease.

Exopolysaccharides: Water-soluble polysaccharides (gums) produced extracellularly by a range of microorganisms. These exopolysaccharides have novel and unique physical properties, and have found a wide range of industrial applications. *See also* Xanthum gum, Gellan gum, Alginate, Dextran, Polytran, Pullulan.

Exothermic reaction: A chemical reaction during which heat is released into the surroundings. Thus no energy input is required, and under appropriate conditions the reaction will occur spontaneously and reach completion. A reaction with a negative enthalpy change. Microbial growth is often exothermic, and therefore fermentors are normally fitted with cooling facilities to remove excess heat and so maintain constant temperature. *Compare with* Endothermic reaction.

Explant: A piece of tissue used to initiate a tissue culture.

Exponential phase: *See* Log phase.

Expression vector: A cloning vector designed such that an inserted gene is expressed (i.e., transcribed into mRNA, which then directs the synthesis of protein at the ribosome) in the host organism. This essentially involves ensuring that the cloned gene is under the control of a promoter sequence appropriate to the host organism, and that the gene is read by the RNA polymerase in the correct reading frame.

Extinction coefficient: An obsolete term in spectrophotometry. *See* Absorption coefficient.

Extraction factor: A factor that determines the degree of separation of a solute in liquid–liquid extraction and is defined as:

$$E = \frac{DV_s}{V_f}$$

where D is the distribution coefficient, and V_s and V_f are the volumes

of solvent and feed, respectively. In continuous processing these volumes may be replaced by the respective flow rates.

Extractive distillation: The addition of a third component to a mixture to decrease the volatility of one of the components and thus allow the separation of mixtures that otherwise would not be separated by distillation. *See also* Azeotropic distillation.

Extractive fermentation: A fermentation process by which the broth is continuously removed from the reactor and the product extracted by a solvent or solution that is immiscible with the fermentation broth and with which the product has a partition coefficient greater than one. The extracted broth (raffinate) is then returned to the fermentor. The advantage of this system is that the product can be removed before any feedback limitation on growth rate occurs. However, it is not frequently used because there are few suitable solvent systems with necessary solubility properties that do not themselves interfere with the fermentation process. *See also* Adsorption fermentation.

F_{ab}: *See* Immunoglobulin G.

Facilitated membrane transport: A process that defines the transport of a substance across a membrane with the aid of a carrier molecule. The carrier molecule is confined to the membrane, but is able to complex with the transferring substance on the outside of the membrane. The molecule then moves across the membrane to the opposite side, where the complex dissociates and releases the transferred substance. The carrier molecule is then able to return to the feed side and repeat the process. The rate of transfer follows saturation kinetics with a leveling of rate at high concentrations of transferred molecules, as there is only a finite concentration of the carrier molecules available. Facilitated transport has been demonstrated in the transport of D-glucose across membranes of vertebrate erythrocytes, with proteins termed permeases or translocases as the carriers.

Facultative: Adjective describing an organism that can grow in the presence or absence of an environmental factor. *See also* Facultative anaerobe.

Facultative anaerobe: An organism, usually a bacterium or fungus, that can adapt its metabolism to enable it to survive and grow in either the presence or absence of oxygen. *See also* Anaerobe, Obligate anaerobe.

Falling-film evaporator: An evaporator in which the feed solution falls under gravity as a film down the walls of the tubular heat exchangers. The vapor–liquid separation usually takes place at the bottom of the heat exchanger. The pressure drop across the tubes is usually very small, and so the boiling point is substantially the same as the vapor head temperature. Hence the evaporator is used to concentrate heat-sensitive materials, and is also useful for the processing of foaming liquids.

Fast-atom bombardment: A technique used to produce mass spectra of difficult-to-volatilize substances such as peptides and nucleotides, or thermally unstable compounds. The procedure involves the bombardment of a metal plate coated with the sample by a stream of fast atoms. The kinetic energy of these atoms is dissipated in a number of ways, some of which lead to the volatilization and ionization of the sample. By maintaining an appropriate electric gradient from the plate, either positive or negative ions can be passed into the mass analyzer. Fast atoms (normally helium, argon, or xenon) are produced by ionizing the appropriate gas and accelerating the ions through an electric field. These fast ions are then fed into a gas chamber, where they collide with atoms of the same gas. Charge exchange occurs as shown. It provides a stream of fast atoms, the majority of which retain the direction and energy of the original fast ions. Any excess fast ions and other ions produced by this charge exchange can be removed, leaving a beam of fast atoms.

$$Xe^{+\cdot}\,(\text{fast}) + Xe \rightarrow Xe\,(\text{fast}) + Xe^{+\cdot}$$

Fast protein liquid chromatography (FPLC): A commercial variant of HPLC systems used for protein separation and recovery.

F_c: *See* Immunoglobulin G.

Fed-batch culture: A system intermediate between batch and continuous processes. The term describes batch cultures that are fed continuously, or sequentially, with fresh medium without the removal of culture fluid.

Feedback (process control): The use of a reaction variable as a control function to influence the reaction.

Feedback control: A closed-loop system for controlling a continuous process, in which control is exercised by the generation of an error signal that operates on the control functions. The error signal is a

measure of the discrepancy between the actual behavior of the system at any instant and the preassigned nominal behavior. This system is capable of reacting retroactively to departures from nominal behavior that have already occurred. *See also* Anticipatory control, Feedforward control.

Feedback inhibition: A control mechanism in which the activity of an enzyme associated with an early step of a multistep pathway is inhibited by a product produced farther along the pathway.

Feeder callus: *See* Nurse callus.

Feeder layer technique: A method for culturing single-plant protoplasts. Protoplasts in low density are spread on filter paper or film mats placed on layers of feeder-plant cells. In this way single cells receive growth factors produced by the feeder cells, as well as growth factors from the nutrient medium. Under these conditions protoplasts synthesize cell walls. Then cell division is initiated; cell division ultimately results in callus formation. The method is also used in animal-cell culture.

Feedforward control: A system for controlling a continuous process. It is based on the measurement of disturbing influences that precede any deviation from the controlled condition, so that corrective action can be taken before any deviation occurs. The system requires a precise model of the effect of the disturbing influence on the controlled condition and of effects of control-parameter adjustments on the process. *See also* Anticipatory control, Feedback control.

Fermentation: To the biochemist, a metabolic process whose main purpose is the conservation of free energy via ATP synthesis that uses substrate-level phosphorylation rather than oxidative phosphorylation. To the microbiologist or biotechnologist, any process that produces a useful product by the mass culture of microorganisms. The required product may be microbial cells (biomass), enzymes, metabolites, or the modification of compounds. Because of the different usage of this word by biochemists and microbiologists, many journal editors do not allow the use of this word in research papers.

Fermentation beer: A term used, particularly in the United States, to describe a fermentation broth after removal of cell debris (i.e., after filtration).

Fermentor (fermenter): A vessel in which organisms can be grown

under sterile and controlled conditions that are optimum for product formation.

Ferromagnetism: A magnetic property of a substance that arises from the cooperative effects of unpaired electrons and is indicated by a very large interaction between the substance and an applied magnetic field. The phenomenon occurs only in the solid state in materials such as metals and metal oxides. Ferromagnetic materials like iron oxides have been used as a filler for ion-exchange resins and in enzyme encapsulation to provide easy and rapid settling on application of a magnetic field. The magnetic properties of substances can be used as aids to separation in downstream processing.

***Ferrovibrio**: See Leptospirillum ferrooxidans.*

FET: *See* Field effect transistor.

Fetal calf serum: Serum collected from a calf fetus. It is an essential component of many mammalian tissue- and cell-culture media because it contains many important growth factors, attachment and spreading factors, and low-molecular-weight nutrients essential for cell growth. Because of the nature of its source and the great demand for use in tissue-culture laboratories, fetal calf serum is expensive. Because of the expense and the problem of batch variation of different samples, considerable effort is being put into the development and production of chemically defined serum-free growth media.

Ficin (E.C. 3.4.22.3): A thiol protease (MW 25,500) produced by water extraction of the latex of figs. It is the least used of the commercially available thiol proteases (the others being papain and bromelain), but has been used as a chillproofing enzyme.

Fick's law of diffusion: A general law that relates the concentration of a substance with distance from a boundary and is applicable for all types of diffusing systems (i.e., liquid, gas, solid, or membrane). The law is normally stated in terms of the rate of diffusion in a given direction (flux, N), as a function of the concentration gradient (dC/dx):

$$N = -D\,(dC/dx)$$

where D is the diffusivity of the diffusing substance and x is the distance in the direction of diffusion.

Ficoll: A nonionic synthetic polymer of sucrose, MW ≈ 400,000. Par-

ticularly used as a density-gradient centrifugation medium and in two-phase aqueous partitioning.

Field effect transistor (FET): The electronic component of miniaturized electrochemical-type sensors. These sensor "chips" (≈30-μm diameter) are similar to those used in computers, except that the metal "gate" that controls the transistor current is replaced by an organic or biochemical material to produce modified FET (MOSFET) or ChemFET. The response of the sensing material to a change in environment has a field effect on the source to drain current off the field effect transistor. This current is usually held at a fixed value while the voltage change from the gate necessary to maintain the current is monitored. *See also* ChemFET.

Film boiling: A type of boiling phenomenon that results in a continuous film of vapor that periodically collapses into the bulk of the liquid.

Filter aids: Substances, often diatomaceous earths, that contain large noncompressible particles; added to a fluid to increase the filtration rate. Filter aids are particularly useful with finely divided solids and slimy flocs. The filter aid should be of low bulk density to minimize the settling tendency, and should also be porous and chemically inert to the system. By providing a bulky precipitate, the filter aid prevents blinding (clogging) of the filter. *See also* Diatomaceous earth, Fullers earth, Kieselguhr, Montmorillonite.

Filtration: A process used in downstream processing for the removal of solids from fluids. As an alternative to centrifugation, filtration generally requires a lower capital investment. However, this advantage is often offset by higher operating costs. A number of different designs and operating regimes are described under separate headings. *See also* Crossflow filtration, Dead-end filtration, Membrane filtration, Microfiltration, Tangential-flow filtration, Ultrafiltration.

Filter press: A device, of which there are several designs, for pressurized filtration. Pressure greater than atmospheric is provided at the filter surface by a liquid pump or gas pressure. Advantages include increased filtration rate and a large filtration area per unit area of floor space. *See also* Plate and frame filter.

Fimbriae: Short filamentous structures on a bacterial cell that are not involved in motility, but have a function in assisting the cell to adhere to surfaces.

Flagellum: A long thin helical structure attached to the bacterial cell at one end and free at the other. The movement of the flagellum gives the cell motility.

Flash chromatography: A modification of column chromatography in which the separation process is accelerated by the use of external pressure on the eluting solvent. External pressure also speeds the flow through the column. The pressures involved are relatively low, so no major modifications of the equipment are required.

Flash evaporator: A device in which the feed solution is fed into a container held at a temperature above the boiling point of the solvent, so that rapid evaporation of the solvent occurs. The device may also operate under a reduced pressure to lower the required temperature of the boiler. Used in particular for solvent recovery from downstream processing raffinates.

Flash fermentation: A method of removing volatile products from a fermentor by circulating the broth from the fermentor to a vacuum chamber where volatiles are removed. Used for ethanol production.

Floc: An association of suspended solids to provide loose aggregates of larger bulk than the original particles.

Flocculation: A process of agglomeration of fine particles in a fluid dispersion to facilitate the separation of the solid particles by either sedimentation or filtration. Small particles settle very slowly in a fluid. However, if they can be gathered together into larger agglomerates (floc), the rate of sedimentation increases and the resulting sediment is less dense and easier to filter. Some systems will readily flocculate with gentle agitation, but others require the addition of chemicals. For example, aluminium sulfate, alum, and ferrous sulfate are used in water treatment; phosphoric acid is used in single-cell protein production.

Flotation: A technique for the separation of solids from liquids whereby gas bubbles introduced into the suspension attach to the solid particles. The particles are carried to the liquid surface, from which they can be removed. The gas, often air, may be blown through the liquid as a stream of fine bubbles. In an alternative two-stage process the gas may be dissolved in the liquid under pressure and then, when the pressure is released, the gas nucleates on the suspended solids.

Flotation reagent: A surface-active substance that, when added in trace amounts to a suspension of solids in a liquid, promotes the attachment of gas bubbles to particular solid particles and thus aids flotation. Other reagents may also be added to increase the stability of the resulting foam and to facilitate the removal of the froth of solids.

Flow cytometry: A technique used to sort cells or chromosomes in a mixed population. For example, a suspension of metaphase chromosomes, released from mitotic cells of an appropriate cell line, is first stained with either one or two fluorescent dyes, depending on whether the machine is single- or dual-beam. (If cells are to be separated, the desired cell type is first labeled with a specific fluorescent dye or substrate.) As the chromosomes pass through a flow chamber they are illuminated (laser beam) and the fluorescence emission, which differs for each chromosome, is measured. The chromosome suspension continues through the flow chamber and exits from the machine as a high-speed liquid jet through a small-diameter orifice (5–10 μm). If the laser beams have detected the particular chromosome of choice (e.g., chromosome 5), a short-voltage pulse applied to the emitting jet electrically charges the droplet containing the chromosomes. This droplet then passes between two charged plates, is deflected away from the waste-collection vessel, and is collected. In this way droplets containing chromosome 5 are collected, whereas other droplets containing unwanted chromosomes (or no chromosomes) go to waste. Two chromosome types can be sorted at once from the same input sample, with each deflected from either side of the waste-collection vessel. Flow cytometric data are usually displayed as a frequency distribution (i.e., a histogram) showing the number of events detected as a function of either one or two fluorescence intensity values, depending on whether one or two dyes are used. This display is called a flow karyotype, by analogy with the karyotype of the cytogeneticist.

Flow injection analysis: A rapid method of continuous quantitative analysis in which the sample is injected into a continuous carrier system in small-bore tubing. The sample and solution are pumped at constant velocity. Various analytical processes (such as reagent addition, dialysis, and solvent extraction) can be carried out as required before the carrier stream and sample are passed through a flow-through cell in an appropriate detector. With automatic injection, this technique can be used to process large numbers of samples.

Flow karyotype: *See* Flow cytometry.

Fluidization: A process by which solid particles may be suspended in a vessel by the upflow of a fluid (liquid or gas). The fluid flow results in an expansion of the bed of particles until, at high flow rate, the particles become entrained and are lost from the reactor.

Fluidized-bed reactor: A reactor whereby the upward passage of a fluid maintains the solid particles (for example, immobilized enzyme particles or microbial cells on an inert support) within the fluid. This allows good mixing of the reactants and minimizes channelling of the bed, with resulting loss of reaction efficiency.

Fluorescein diacetate (FDA): A stain commonly used to determine cell viability. FDA is absorbed by cells, and esterase activity within the cells deacetylates the dye, which becomes fluorescent. Cells are viewed under a microscope with an ultraviolet attachment. Viewing of cells on a light microscope with white light illumination reveals all cells, whereas ultraviolet illumination reveals only "living" cells, which fluoresce brightly. *See also* Dye exclusion tests.

Fluorescence: A molecular process whereby radiation is emitted from a substance after stimulation by adsorption of radiation. The adsorption of radiation promotes electrons within the molecule, which then return to the ground state by a series of processes, one of which produces the emitted fluorescence. The emitted radiation may be in the visible or ultraviolet region but, because of the electronic processes involved, the wavelength emitted will always be greater than the wavelength absorbed. The emitted radiation is always measured perpendicular to the incident radiation to eliminate interference. Once the incident radiation is removed, fluorescence ceases (unlike phosphorescence emission).

Fluorimetry: An analytical technique that uses the process of fluorescence. Because of the nature of fluorescence and the limitation placed on the types of molecule that exhibit fluorescence, the technique can be highly selective and very sensitive. Unlike other common spectroscopic techniques, the intensity of fluorescence is related to the intensity of the incident radiation. This relationship provides a useful instrumental variable. An additional advantage is that sterilizable probes are now available so that fermentor profiles can be obtained for compounds like NAD(P)H, which will fluoresce at 460 nm following radiation at 340 nm. The system is responsive to NAD(P)H levels within the cell and thus provides a very useful detection system for monitoring certain forms of biomass within a fermentor.

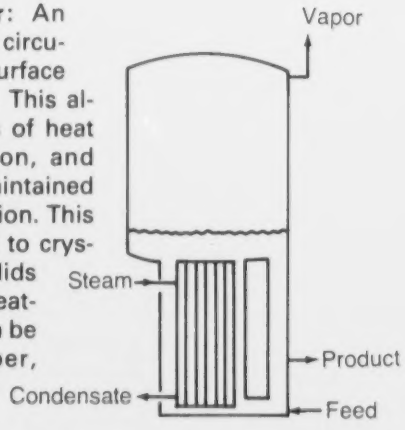
Fluorography: The introduction of a scintillant, or "fluor" into a gel or on the surface of a chromatogram, such that low-energy emitters (such as β-emissions from ^{3}H-labeled materials present in the gel or chromatogram) can be detected by using a photographic film. These β-emissions cannot pass through a gel or even through the protective coating of an X-ray film. By converting this energy to visible light by interaction with a scintillant, the light produced can penetrate the gel and film coating and leave a latent image.

Flush end: *See* Blunt end.

Flux: A kinetic parameter that measures the rate of transport across fluids, membranes, etc.

Foam: An aggregation of gas bubbles and liquids forming a stable raft on the surface of a liquid. Foaming is a problem in fermentor design that requires chemical addition and occasionally mechanical devices to prevent excessive foaming with loss of fermentor contents. *See also* Antifoam agents.

Forced-circulation evaporator: An evaporator in which the liquor is circulated across the tubular heated surface by means of a circulating pump. This allows separation of the functions of heat transfer, vapor–liquid separation, and crystallization. Circulation is maintained regardless of the rate of evaporation. This type of evaporator is well suited to crystallization operations, because solids will not settle out and plug the heating tubes. The heat exchanger can be placed inside the feed chamber, where scaling of the exchanger tubes is not a problem.



Forced convection: The relative movement of fluid elements caused by external forces such as mechanical stirring or air sparging. *See also* Free convection.

Forward mixing: In fluid transport, the phenomenon in which some elements of the fluid are accelerated relative to the average element

and thus have a reduced residence time in the reactor. Forward mixing leads to a reduction in reactor efficiency, as optimum residence time is not achieved. Forward mixing can be experienced where elements short-circuit the normal flow pattern in, for example, packed columns. *See also* Axial mixing, Back mixing.

Fouling: The deposition of material onto surfaces that may result in an eventual breakdown of the process. Membranes, filter cloths, and devices containing small holes are particularly vulnerable to fouling. In fermentors, fouling by deposition of biomass, proteins, polysaccharides, etc., can cause problems with heat exchangers, baffles, and interior exposed walls.

Frameshift mutation: An alteration in the structure of DNA that results in a change of the reading frame (triplet code) being used by the enzyme RNA polymerase. As a result of this mutation, the amino acid sequence of the protein coded for by the region of DNA containing the mutation is completely altered beyond the point of mutation and normally results in the production of a "useless" protein.

Free convection: The relative movement of fluid elements under the influence of variations in the natural environment (e.g., temperature, concentration). *See also* Forced convection.

Freeze-drying: A process in which a solvent, often water, is removed by sublimation from the frozen state. Because the vapor pressure of the frozen solvent is considerably below atmospheric pressure, freeze-drying requires the use of high vacuum. The technique is used widely to concentrate and dry materials that cannot be dried satisfactorily by other methods. The advantages of freeze-drying include maintenance of sterile conditions, no foaming, and minimal loss of volatile and labile products because of the low temperatures involved. Also termed lyophilization when the solvent is water. *See also* Culture maintenance, Lyophilization.

Freezing and thawing: A method sometimes used for breaking cells. Ice crystals formed in the frozen cell rupture the cell wall or membrane. Rather time-consuming and not a particularly efficient method.

Freundlich isotherm: An equation relating the quantity of material adsorbed on a surface (q) with that in solution (c) at constant temperature. It is applicable to adsorption where there is an exponential distribution of heats of adsorption.

$$q = k_F c^{\beta}$$

where k_F is the Freundlich constant. When $\beta > 1$, the isotherm is favorable to adsorption; when $\beta < 1$, the isotherm is unfavorable to adsorption.

Freund's adjuvant: *See* Adjuvant.

Froude number: A dimensionless group that relates rotational inertial forces with gravitational forces acting on an element of the fluid. It involves the rotational speed of the impeller (N) in revolutions per minute and the impeller diameter D_i:

$$Fr_i = \frac{N^2 D_i}{g}$$

where Fr_i is the Froude number and g is the gravitational constant. It is applied to unbaffled tanks and reactors, because in baffled systems Fr_i is insignificant, as vortexing is negligible and the Reynolds number adequately describes the fluid hydrodynamics. *See also* Reynolds number.

Fullers earth: A type of diatomaceous earth used as a filter aid or adsorbent. *See also* Filter aid, Diatomaceous earth.

Fungi: A group of eukaryotic organisms devoid of chlorophyll. They normally have cell walls of cellulose or chitin and are usually nonmotile, although they may produce motile reproductive cells. Reproduction is commonly by sexual or asexual spores. They do not possess stems, roots, or leaves, nor do they have vascular systems. Most fungi consist of septate or nonseptate filaments (individually called hyphae and collectively called mycelium) whose dimensions can vary considerably. There are two main types of mycelium: septate (when the cells, with one or two nuclei, are separated by cross walls) and coenocytic (lacking septa). Reproductive structures can usually be differentiated from vegetative structures, and the range of distinct forms is used as a basis for classifying fungi into five groups: *Mastigomycotina, Zygomycotina, Ascomycotina, Basidiomycotina,* and *Deuteromycotina.*

Fungi imperfecti: *See* Deuteromycotina.

Fusogen: *See* Chemical fusogen.

Fusion protein: A protein consisting of all or part of the amino acid sequences of two or more proteins, formed by fusing the two protein-

encoding genes. This fusion is often done deliberately, either to put the expression of one of the genes under the control of the strong promoter for the first gene, or to allow the gene of interest (which is difficult to assay) to be more easily studied by substituting some of the protein with a more easily measured function (e.g., by fusing with the β-galactosidase gene, the product of which can easily be measured using a chromogenic substrate).

Fusogenic agent: Any compound, virus, etc., that can be used to fuse cells.

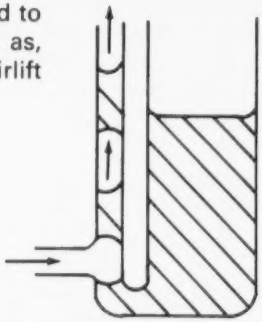
GAG: A region of the RNA of a retrovirus that codes for a structural protein that associates with the RNA in the core of the viral particle. Other retroviral genes are POL and ENV.

Galactans: Polysaccharides, essentially polymers of galactose. *See also* Agar, Carrageenans.

β-Galactosidase: *See* Lactase.

Gas chromatography (GC): A type of chromatographic separation in which the sample, consisting of a mixture of volatile components, is partitioned between the vapor phase and a nonvolatile liquid adsorbed on the surface of an inert matrix. An inert carrier gas transports the components through the column until they reach the detector. GC may be used to monitor components in a process stream or as a means of purification and separation of mixtures or for quantitative analysis.

Gas lift: A device by which a gas flow is used to lift a liquid and thereby promote circulation, as, for example, in airlift fermentors. *See also* Airlift fermentors, Deep-shaft airlift fermentor.



Gasohol: An automobile fuel produced by mixing gasoline (petrol) with ethanol. A particularly attractive approach in developing countries where sucrose-rich plants such as sugar cane and sweet sorghum are readily available as raw materials for cheap ethanol production by fermentation. Brazil, in particular, adopted this approach by establishing and implementing the Brazilian National Alcohol Program. *See also* Ethanol.

Gel: A semisolid mixture of a solid and a liquid, often consisting of a polymeric substance saturated with liquid as, for example, agar, agarose, and silica gels.

Gel electrophoresis: A type of electrophoresis in which ions are transported through a gel under the influence of an electric current. Typical matrices are agarose, starch, and polyacrylamide. The separation factors depend on both the charge–mass ratio and interactions between the charged species and the gel matrix. *See also* Polyacrylamide gel electrophoresis.

Gel exclusion chromatography: *See* Gel filtration.

Gel filtration: Also known as gel permeation chromatography and size exclusion chromatography. A chromatographic purification technique that separates molecules according to size. The column material consists of beads that contain pores of various sizes. As the mixture to be fractionated passes through the column, large molecules are excluded from the pores and enter only the spaces between the beads. These molecules, eluted first from the column, are referred to as the void volume. Smaller molecules that can enter the pores elute in order of decreasing size, because the smaller the molecule,

the greater the number of pores it can enter and thus the longer it will be held on the column. Below a certain minimum size all remaining molecules will elute together, as they are all capable of passing through all the pores. This remainder is referred to as the included volume. Different grades of gel filtration media can be purchased, depending on the fractionation range required. The choice of gel filtration media available includes cross-linked dextrans (Sephadex and Sephacryl) and cross-linked agarose (Sepharose and Bio-Gel).

Gel filtration chromatography: *See* Gel filtration.

Gellan gum: A polysaccharide biopolymer excreted by *Pseudomonas elodea* and commercially available for use in microbiological media as a gelling agent to replace agar. The repeating unit consists of a linear tetrasaccharide. The gum is also a potential alternative source of rhamnose (instead of quercitrin).

Gel permeation chromatography: *See* Gel filtration.

Gel resin: A form of ion-exchange resin in which the polymeric support consists of a polymeric resin (normally cross-linked polystyrene, which has a solid gellike structure). Because there is not a defined pore structure, the resin has a low affinity for large molecules and very poor kinetics of adsorption. In addition, large molecules that enter the structure are difficult to remove. Thus the resins are susceptible to fouling and subsequent loss of capacity. However, the resins have a high capacity for small ions and are used in water purification and softening processes. *Compare with* Macroporous resin.

Geminiviruses: One of the two classes of DNA viruses (the other being caulimovirus) that infect plants. They have potential as cloning vectors in plants.

Gene bank: *See* Gene library.

Gene cloning: The process whereby a gene is inserted into an appropriate vector (e.g., plasmid), which then transports the gene into a host cell (usually a bacterium). Once within the host, the vector produces numerous identical copies of itself and the gene it carries. Division of the host cell produces progeny that all contain vector molecules that can undergo further replication. This process results in the formation of a colony or clone of identical host cells that each contain one or more copies of the gene-containing vector. The gene is now said to be cloned.

Gene library (genomic library): A collection of recombinant clones, which between them contain all the DNA present in a particular organism.

Gene probe: A nucleic acid molecule that can be used to detect, by complementary base-pairing, another nucleic acid molecule that has a complementary or homologous sequence. The probe is invariably labeled (*See also* Nick translation, Biotin) to allow autoradiographic or enzymatic detection of the hybridization reaction. *See also* Colony hybridization, Southern blotting.

Genetic engineering: A very broad term, also refered to as gene manipulation or recombinant DNA technology. Defined by the 1978 Genetic Manipulation Regulations as "the formation of new combinations of heritable material by the isolation of nucleic acid molecules, produced by whatever means outside the cell, into any virus, bacterial plasmid or other vector system so as to allow their incorporation into a host organism in which they do not naturally occur, but in which they are capable of continued propagation."

Genome: The complete, single-copy set of genetic instructions for an organism.

Genomic library: *See* Gene library.

Germ cell: The male and female reproductive cells; egg and sperm in mammals, ovum and pollen in plants.

Germplasm: An old term used to describe an unidentified material transmitted from generation to generation through the gametes. Essentially referring to genes.

Germplasm storage: Plant-breeding programs are generally based on adapting ancient plant varieties and their relatives. As plant-breeding programs proliferate, there is a danger that this original genetic information will be lost as these ancient varieties are replaced by modern varieties. Attempts are therefore being made to preserve the genotype (germplasm) of such species. This is most easily done by cryopreservation of shoot tips, embryos, and meristems.

Gibberella fujikuroi: A fungus, belonging to the Ascomycotina, grown in submerged culture to produce the secondary metabolite, gibberellic acid.

Gibberellic acid (GA_3): One of a group of naturally occurring plant hormones, the gibberellins, that have a complex chemical structure containing a gibbane nucleus with four cyclic carbon rings. Although gibberellins have been isolated from plant materials, the best source is from the fungus *Gibberella fujikuroi*, grown in submerged culture. *See also* Gibberellins.

Gibberellins: Plant-growth substances related to gibberellic acid (GA_3). They are diterpenoids containing four cyclic carbon rings and all have the ability to cause stem elongation when applied to intact plants in the light. Many endogenous gibberellins have been found in plants. Other synthetic plant-growth substances have been prepared from gibberellic acid. Gibberellic acid, a metabolic product of the fungus *Gibberella fujikuroi*, can be obtained from the fungal growth medium.

Glucans: Polysaccharides composed of D-glucose units. They can have either straight or branched chains. The glycosidic linkages can be α-1,4 as in amylase and dextran, β-1,4 as in cellulose, β-1,3 as in cellose, or 1,6 as in pustulan. Branched glucans include amylopectin and dextran.

Glucoamylases (amyloglucosidases): Exoamylases (i.e., enzymes that cleave off terminal sugar residues) produced commercially from *Aspergillus* spp. or *Rhizopus* spp., both of which produce the enzymes extracellularly. They have low specificity, hydrolyzing α-1,4 glucosidic bonds in branched oligosaccharides and, at a slower rate, α-1,3 and α-1,6 bonds. Principally used in the saccharification of starch to produce high-glucose syrups.

Glucose isomerase: *See* High-fructose syrups.

Glucose oxidase: An enzyme that catalyzes the reaction:

$$\beta\text{-}\delta\text{-glucose} + O_2 \rightarrow \text{D-glucose-1,5-lactone} + H_2O_2$$

The enzyme is used extensively as an antioxidant in the food industry, usually in conjunction with catalase. The catalase consumes the H_2O_2 produced during the oxidation reaction, which would otherwise denature the enzyme. Commercial sources of the enzyme are derived from *Aspergillus niger*, *Penicillium glaucum*, and *P. notatum*. The enzyme is used to prevent changes in the color and flavor of foods during processing, transportation, and storage (e.g., in beers, wines, sauces, citrus fruit drinks, cake mixes, and instant soup).

Glucose syrup: Purified, concentrated aqueous solutions of glucose and higher saccharides produced by the hydrolysis of corn (maize) or potato starch. Syrups are classified according to their dextrose equivalent (DE), which is a measure of the extent of starch hydrolysis. Used as a sweetening agent in sugar confectionery. Also referred to as corn syrup, corn starch hydrolysate, starch syrup, and confectioners' glucose.

Glutamate: *See* Glutamic acid.

Glutamic acid (glutamate): An amino acid of considerable importance to industry as a feed and food supplement, particularly as monosodium glutamate, which is used as a flavor enhancer. It is produced industrially by the growth of *Corynebacterium glutamicum* or *Brevibacterium divaricatum*, using starch hydrolysates, molasses, ethanol, or acetate as substrate. Worldwide production is over 100,000 tons per year.

Glutelins: One of the four major categories of seed storage proteins.

Glycocalyx: A general term for polysaccharide components outside the bacterial cell wall. *See also* Capsule, Slime layer.

Glycoprotein: A protein containing one or more covalently linked carbohydrate moieties. The carbohydrate moiety can be either a single sugar residue or a chain (linear or branched) of the same or dissimilar sugar residues. Linkage to the protein is invariably via the side chain of an asparagine, serine, or threonine residue.

Glycosidases: A group of hydrolases that attack glycosidic bonds in carbohydrates and glycoproteins. *See also* α- or β-Amylase, Cellulase, Glucoamylases, Invertase.

Gram stain: An important differential stain (introduced by Christian Gram) used to separate bacteria into two groups, Gram-positive and Gram-negative. Cells are first stained with crystal violet, washed, and treated with an iodine solution. Iodine forms a complex with crystal violet and stains the cells a purple-blue. The stained cells are washed with alcohol or acetone. The stain complex will not be removed from the walls of some bacteria (Gram-positive). After decolorization, a red counterstain, such as basic fuchsin or safronin, is used to stain Gram-negative cells red and make them easier to detect under microscopic examination. The Gram stain is thought to become trapped in pores of the mucopeptide of the cell wall during dehydration with alco-

hol. In Gram-negative cells the mucopeptide layer is thinner. The difference in mucopeptide layer is responsible for the difference in ease of rupturing Gram-positive and Gram-negative bacteria. Gram-negative cells are most easily broken, being lysed by low levels of detergents such as sodium dodecyl sulfate (SDS) or isooctylphenoxypolyethoxyethanol (Triton X-100), whereas Gram-positive cells need lysozyme treatment first.

Granum: *See* Thylakoids.

GRAS organisms: Selected strains of molds, bacteria, and yeasts are currently used as sources of enzymes for food processing. The most commonly used are *Aspergillus oryzae*, *Aspergillus niger*, and *Bacillus subtilis*. These three organisms are members of a small group that the Food and Drug Administration (FDA) rated "generally recognized as safe" (GRAS) for use in the food industry. They are therefore the preferred organism of choice for a given situation, because inadvertent contamination of foodstuffs by these organisms or their products should not present a human health threat. However, the use of several other organisms as sources for specific enzyme preparations has been approved by the FDA (e.g., *Mucor miehei* for the production of rennet).

GRASE: "Generally recognized as safe and effective." Under the Federal Food, Drug, and Cosmetic Act, before a new drug for human consumption is allowed on the market, experts in the field must find it GRASE for uses recommended by its labeling. This finding involves examination of the safety and efficiency of the drug, based primarily on clinical tests on human subjects.

Grashof number: A dimensionless group associated with mass transfer by natural convection:

$$\mathrm{Gr} = \frac{L^3 g \Delta \rho_A}{\rho \nu^2}$$

where L is length of the system; g is gravity; ρ is density; $\Delta\rho_A$ is density difference of A between two points in the transfer field; and ν is kinematic viscosity of the fluid.

Griseofulvin: A nontoxic systemic antifungal antibiotic originally detected in cultures of *Penicillium griseofulvum*, but commercially produced using *P. patulum*. Griseofulvin, with a fungistatic mode of action against fungi other than yeasts and the mastigomycotina, is

used in treatment and control of fungal diseases of the hair, skin, and nails. It is thought to interfere with chitin synthesis in growing hyphae.

Growth hormone: *See* Human growth hormone.

Grunstein–Hogness method: *See* Colony hybridization.

5′-Guanylate (guanosine monophosphate, GMP): A flavor enhancer produced industrially in several ways: (1) by the action of nuclease (5′-phosphodiesterase) from *Penicillium citrinum* or *Aspergillus* spp. on yeast RNA, (2) by chemical phosphorylation of guanosine, (3) by the enzymatic (microbial) conversion of 5′-xanthosine monophosphate to GMP, or (4) by chemical synthesis. Over 1000 tons of GMP is produced annually in Japan.

Habituation: The acquired ability of plant cells to grow and divide independently of exogenous plant-growth substances (hormones).

Hagen–Poiseuille law: *See* Darcy law.

Halophile: A microorganism capable of growing in solutions containing concentrations of sodium chloride greater than about 3%. Such concentrations are toxic to freshwater microorganisms.

Hammer mill: A mechanical device used to shread bulk solid materials (e.g., sugar cane, beet). The device consists of a rotating shaft on which hinged flails or hammers are fixed. The shaft is contained in a shell or cylinder through which the feed material is passed to emerge at the other end in a shredded form.

Haploid: Cells having a single set of chromosomes.

HART: *See* Hybrid arrest translation.

Harvesting: A term used to describe the recovery of microorganisms from a liquid culture, usually by filtration or centrifugation, to give a pellet of microorganisms.

HAT medium: Tissue culture medium (containing hypoxanthine, aminopterin, and thymidine) that is used as a selection medium. For example, nonfused myeloma cells and plasma cells (lymphocytes)

cannot survive in this medium, but fused hybridoma cells can. (*See* Monoclonal antibodies). Similarly, the medium can be used to select transfected mammalian cells by using the thymidine kinase (Tk) gene as a selectable marker for transfected cells. Tk^- cells are used and transfection is achieved by using the Tk gene with the gene or genes of interest linked to it. Tk^- cells die in HAT medium, whereas Tk^+ cells (transfected cells) survive.

Heat exchanger: A device in which heat is transferred from one fluid stream to another without the streams coming into physical contact. One fluid is heated and the other is cooled.

Heat transfer: The input or removal of heat from a process vessel or stream. For example, the performance of bioreactors depends to a large part on the efficiency of heat transfer from the vessel because the maximum growth rate of most microorganisms is achieved only in a narrow range of temperatures that must therefore be maintained. Heat is generated in bioreactor processes from a number of sources, including metabolic energy, mechanical agitation energy, and gassing and aeration energy. Heat is removed by cooling water in internal coils, external cooling jackets, or heat exchangers.

Height equivalent to a theoretical plate (HETP): A measure of the performance of a column contactor, defined as the height of the column that, under the process conditions, is equivalent to a theoretical plate. The theoretical plate is defined as a device at which perfect contact occurs so that the streams leaving it are in equilibrium. HETP is a step function dividing the column into equal portions, unlike the height of a transfer unit (HTU), which is a continuous function.

Height of a transfer unit (HTU): A measure of the performance of a column contactor as used in distillation, adsorption, etc. A transfer unit (N_T) is a dimensionless parameter that relates the column height (h), overall mass-transfer coefficient (k_o), interfacial area of any sorbent species (a), volumetric flow rate of the fluid (F), and column cross-section (s), according to the equation:

$$N_T = \frac{k_o a h s}{F}$$

from which the height of a transfer unit can be calculated:

$$H_T = \frac{h}{N_T} = \frac{F}{k_o a s}$$

The advantage of this parameter is that it includes the ratio of mass transfer coefficient and flow rate, which reduces the problems associated with the variation of the former with flow rate.

Helicase: An enzyme preparation rich in β-1,3-glucanase activity, prepared from snail internal organs, used to degrade yeast cell walls to produce protoplasts.

Hemicelluloses: High-molecular-weight polysaccharides found in the cell walls of higher plants, together with cellulose and lignin. In many plants the major hemicellulose is a polymer comprising about 80% pentoses (of which about 80% are D-xylose) and containing side chains of other sugars and sugar acids.

Hemolysis: The lysis of red blood cells.

Heparin: An acidic mucopolysaccharide from animal tissues capable of interacting with basic residues on the surface of a protein. It consists of equal amounts of D-glucosamine and D-glucuronic acid, α-1,4-glycosidically linked, and also contains O- and N-sulfate links. Heparin inhibits many enzymes involved with nucleic acid metabolism, and has been used as an affinity ligand for the purification of many such enzymes (e.g., DNA and RNA polymerase, ribonuclease, restriction endonucleases, and DNA topisomerase). Heparin also inhibits blood clotting by inhibiting the conversion of prothrombin to thrombin and fibrinogen to fibrin. It is therefore used in the collection of whole blood and in other chemical situations, such as in heart–lung machines. The fractionation of heparin to produce a group of new oligosaccharides with reduced risk of hemorrhage while maintaining antithrombotic efficacy has been investigated with *Cytophaga heparina*. Some fractions have been found to possess additional fibrinolytic and tumor-growth-inhibiting activities.

Herschel–Buckley equation: A rheological equation applicable to plastic flow, which relates the applied stress (τ) to the shear rate (γ) in the form:

$$\tau = k\gamma^n + \tau_o$$

where τ_o is yield stress and k is a constant.

Heteroduplex: A DNA molecule formed by base-pairing between two DNA strands that are not completely complementary. *See also* Cross hybridization.

Heterofermentative: A term normally used to describe a bacterial culture that ferments glucose or another sugar to lactic acid and other products, usually carbon dioxide and ethanol. *See also* Lactic acid bacteria. *Compare with* Homofermentative.

Heterokaryon: A cell in which two (or more) nuclei, originating from different cell types, are present in a single cytoplasm. If the two nuclei fuse, the heterokaryon develops into a hybrid cell.

Heterotrophs: Organisms that require preformed organic molecules as their source of energy or substrates for biosynthesis. They include animals, fungi, and most (but not all) bacteria. *Compare with* Autotrophs.

HETP: *See* Height equivalent to a theoretical plate.

Heurty process: *See* Whey.

Hevea brasiliensis: A cultivated plant that is the source of natural rubber. Latex obtained from this plant contains hydrocarbons in the molecular weight range $1–2 \times 10^6$.

Hierarchical control: The use of a computer to oversee the control functions of other computers, which are themselves controlling individual parts of a process.

High-fructose syrups (HFS): Solutions containing high fructose proportions, prepared by the isomerization of glucose. The enzyme glucose isomerase will isomerize glucose (which has only 65% of the sweetness of sucrose) into a mixture of fructose (>50%), glucose, and other sugars (high-fructose syrup or isoglucose). Fructose is about 1.5 times sweeter than sucrose. Because glucose can be prepared readily from starch, HFS has been replacing sucrose in many food applications. The process is particularly attractive in countries where starch crops are in abundance but locally produced sugar is in short supply or absent, or where sucrose costs are high (often unrealistically high as a result of farm subsidies). Glucose produced by starch hydrolysis is used as the starting material for HFS production. Microorganisms most commonly used for the production of glucose isomerase are *Bacillus coagulans*, *Actinoplanes missouriensis*, *Arthrobacter* spp., and *Streptomyces* spp. Either the extracted enzyme is used in an immobilized form, or immobilized whole cells that contain the enzyme are used. Further enrichment using industrial-scale chromatography can give syrups containing up to 70% fructose. Over 5 million tons of HFS is currently produced annually worldwide.

High-performance liquid chromatography (HPLC): A general term describing high-resolution column chromatographic techniques. Improvements in the nature of column-packing materials for a range of chromatographic methods (e.g., gel filtration, ion exchange, reverse phase) has yielded smaller rigid beads with greater uniformity in size and shape. This improvement allows packing in columns with minimum spaces between beads and thus minimizes peak broadening of eluted molecules caused by diffusion within these spaces. Minimum peak broadening results in considerably increased resolution over the more conventional soft gels. Because of the close packing of spheres, high pressure is needed to pump solvents through the column, so columns are packed in stainless steel tubes. Because of this need for high pressure, HPLC is often inadvertently referred to as high-*pressure* liquid chromatography.

High-rate filter: *See* Percolating filter.

hn RNA: Heterogeneous nuclear RNA. *See also* Introns.

Hofmeister series: The arrangement of anions in order of their efficiency in salting out of hydrophilic colloids. The anions in this series possess strong dehydrating properties and so can precipitate hydrophilic colloids. Also termed lyotropic series.

Hollow-fiber reactor: A reactor design, particularly used for immobilized enzymes and the growth of mammalian cells. Hollow fibers are packed into bundles within a cylindrical vessel. Nutrient is delivered through the lumen of each fiber while the cells grow in the extracapillary space. Fibers can be made from a range of porous semipermeable membranes. The pore size is small enough to retain cells, but large enough to allow the passage of nutrients and waste materials.

Holoenzyme: *See* Cofactor.

Homofermentative: Normally used to describe a bacterial culture that ferments glucose or another sugar to lactic acid as a single product. *See also* Lactic acid bacteria. *Compare with* Heterofermentative.

Homology: The degree of identity between two nucleotide sequences. For example, 95% homology indicates that 95 nucleotide positions out of 100 are identical in the two sequences.

Homopolymer tailing: A method for producing sticky ends in a DNA molecule by adding a polymer of identical nucleotides (e.g., poly-

deoxycytosine) to the 3′-OH termini by using the enzyme terminal transferase in the presence of a single deoxynucleotide. This enzyme allows the DNA fragment to be linked to an appropriate vector by complementary base-pairing where the appropriate homopolymer (in this case polydeoxyguanosine) has been added to the vector by the same technique.

HPLC: *See* High-performance liquid chromatography.

HTU: *See* Height of a transfer unit.

Hughes press: A device used to disrupt cells before downstream processing. It operates by forcing a frozen cell paste through a small orifice under high pressure. This method of cell disruption is normally confined to laboratory scale.

Human growth hormone (somatotropin): A 191-residue protein (MW 22,000) produced in the anterior pituitary gland and needed for longitudinal growth of the skeleton. Growth hormone deficiency results in dwarfism. Originally in very short supply, as it had to be purified from cadaver pituitaries, it is now being produced from *Escherichia coli* by recombinant DNA technology. Unlike other clinically useful products produced by recombinant technology (e.g., insulin and interferon), the world market for the material is not great. However, the hormone may also be of value in treating burns, wounds, and fractured bones. These applications would considerably enhance the market for the genetically engineered product.

Humectants: Substances that absorb moisture. They are used to maintain the water content of materials such as baked products, tobacco, and glue. Examples are glucose syrup, invert sugar, and honey.

Humic acid: A group of naturally derived organic acids of high molecular weight and varying structure present in soils, peat, etc., and forming the coloring matter in surface waters. Often the cause of fouling of ion-exchange resins and other adsorbents used in raw-water treatment.

Hyaluronic acid (HA): A glycosaminoglycan forming part of the connective-tissue matrices of all vertebrates, and also found as part of the capsular material that surrounds *Streptococcus* spp. It is a viscoelastic biopolymer that has great importance in ophthalmic surgery, where it is used to replace the aqueous humor of the anterior chamber during cataract surgery and intraocular lens implantation.

HA is also a major component of synovial fluid, can be used to replace fluid lost during joint surgery, and is used to treat joint inflammation. HA has considerable potential in the health care and cosmetic industry. The main source of HA at present is extraction from rooster combs, but a number of processes that produce HA by the fermentation of streptococci are also in use.

Hybrid arrest translation: A method for identifying the protein coded for by a cloned gene. The denatured cloned gene is mixed with an mRNA population and will base-pair with its corresponding mRNA. The mRNA population is then translated in an in vitro protein synthesis system, and the protein products are identified by gel electrophoresis and autoradiography. This experiment is repeated with the mRNA population *without* the added gene. It will give the same protein pattern, but with an extra protein band. This extra protein is the protein encoded for by the cloned gene.

Hybrid release translation: A method for identifying the protein coded for by a cloned gene. The denatured gene is immobilized on nitrocellulose and an mRNA population is passed through the filter. The DNA will base-pair with its corresponding mRNA, whereas other mRNA species do not bind. The DNA–RNA hybrid is then dissociated by heating, and the mRNA is translated in an in vitro protein synthesis system. The protein product, identified by immunoprecipitation or gel electrophoresis and autoradiography, represents the protein encoded for by the cloned gene.

Hybridization: **(1)** Any mechanism that allows the exchange of nuclear material between one cell and another similar but genetically different individual and results in the formation of offspring with genotypes different from either of the parents. In general, hybridization is expressed as sexual hybridization in eukaryotic organisms and as parasexual hybridization in prokaryotes, most eukaryotic tissue cultures, and certain eukaryotes that do not exhibit true sexuality.

: **(2)** The formation of a double-stranded molecule by complementary base-pairing between two single-stranded DNA molecules, or a single-stranded DNA molecule and an RNA molecule. *See also* Gene probe.

Hybridization probe: *See* Gene probe.

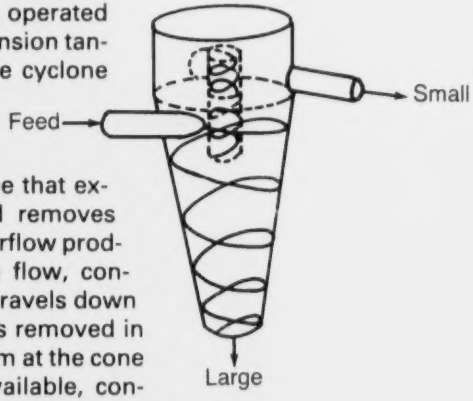
Hybridoma cell: An immortalized antibody-secreting cell line created by fusing an antibody-secreting plasma cell (lymphocyte), which is producing the desired antibody, with a myeloma cell line (an immortal

antibody-secreting tumor cell). The myeloma cell line used is usually a mutant that has lost the ability to produce its own antibodies, so that the resultant hybridoma cell line secretes only the antibody that is desired.

Hybrids: *See* Cell hybrids.

Hydrocolloids: A class of food additives used to enhance the physical properties of food by their ability to thicken and form gels. Compounds used include bacterial polysaccharides from *Pseudomonas* spp. and xanthan gum.

Hydrocyclone: A device for the separation–concentration of particles in suspension in a fluid. It is operated by pumping the fluid suspension tangentially into the top of the cyclone to produce a centrifugal action and vortexing. The cover of the cyclone has a downward-extending tube that extends into the vortex and removes part of the stream as an overflow product. The remainder of the flow, containing most of the solids, travels down the walls of the cone and is removed in a partially concentrated form at the cone apex. Various sizes are available, constructed of materials that include plastics, ceramics, and metals. Advantages are low capital cost and the ability to make separations based on small differences in particle size.



Hydrophilic: *See* Lipophobic.

Hydrophobic: *See* Lipophilic.

Hydrophobic chromatography: A chromatographic separation technique for proteins based on the hydrophobic interaction between the protein and the chromatographic support. The support is normally an agarose derivitized with long-chain alkyl hydrocarbon chains to provide a hydrophobic surface. Interaction between these hydrophobic areas and hydrophobic "patches" or "pockets" on the protein provides a means of discrimination, although electrostatic interactions and hydrogen bonding may also be involved. Proteins are

bound to the column matrix in high salt concentration (e.g., 2 M ammonium sulfate) and eluted by decreasing the ionic strength, thereby decreasing the hydrophobic interactions between the column matrix and protein. Proteins are therefore eluted in order of increasing hydrophobicity.

Hydroponics: Water-culture of plants. A plant-culturing system where plant roots are developed not in soil but in a mass of inert particles (usually sand or gravel) that is moistened with a prepared nutrient solution by capillary action. Although this method provides abundant water and nutrients to the plants, aeration of root systems is poor. *Compare with* Nutrient film technique.

Hydroxyapatite: A naturally occurring hydrated calcium phosphate that can be used as a chromatographic support for the chromatographic separation of proteins.

Hyoscyamine: An anticholinergic compound isolated from the plant *Hyoscyamus niger*.

Hyperchromic effect: The observation that the UV absorbance at 260 nm of a solution of single-stranded DNA molecules is approximately 30% more than would be displayed by the same concentration (nucleotides per cubic decimeter) of double-stranded DNA. The heterocyclic rings of DNA absorb at 260 nm, but this absorbance is reduced when the nucleotides are involved in hydrogen bonding and base stacking. The denaturation (melting) of DNA can therefore be monitored by the increase in absorbance at 260 nm, referred to as hyperchromicity.

Hyperchromicity: *See* Hyperchromic effect.

Hyperfiltration: *See* Reverse osmosis.

Hyphae: The basic unit of a fungus. A fungal filament.

Hypochromic effect: The decrease in absorbance at 260 nm observed when single-stranded DNA molecules renature to give double-stranded DNA. *Compare with* Hyperchromic effect.

Hypophase: A term used to denote the more dense phase in a two-phase system, especially where both phases may be similar in nature (e.g., two-phase aqueous systems). *Compare with* Epiphase.

IAA: Indoleacetic acid. *See also* Auxins.

Idiophase: The phase of a culture during which products other than primary metabolites are synthesized. Unlike primary metabolites, metabolites produced during the idiophase have no obvious role in cell metabolism. The metabolites produced during the idiophase are referred to as secondary metabolites.

IgG: *See* Immunoglobulin G.

IMAC: *See* Immobilized metal-affinity chromatography.

Immiscibility: The property whereby fluids form two distinct phases under all relative proportions. *See also* Miscibility, Partially miscible substances.

Immobilization: The conversion of enzymes or cells from the free mobile state to the immobilized state, either by attachment to an appropriate support or by entrapment in an appropriate matrix. *See also* Cell immobilization, Enzyme immobilization.

Immobilized biocatalyst: Enzymes or cells immobilized on a solid support and used to catalyze a biochemical reaction. *See also* Cell immobilization, Enzyme immobilization.

Immobilized metal-affinity chromatography (IMAC): A chromatographic protein purification technique involving the adsorption of the protein to a support matrix as a result of coordination between an immobilized metal ion and an electron donor. Normally the metal ion is immobilized (usually chelated) on a support, and the protein binds to the metal ion(s) via electron-donor group(s) on the protein surface (e.g., cysteine, arginine, and histidine have electron-donor atoms in their side chains). In an alternative but less commonly used approach, the metal ion, immobilized on the protein surface, forms a coordination bond with an electron-donor group attached to the support matrix. Protein is eluted either by changing the pH, by ligand exchange (i.e., eluting the column with competing electron-donor solutes), or by the addition of chelating agents.

Immortalized cells: Cells that show continuous proliferation and can be subcultured indefinitely. Such cells are necessarily malignant in nature. The culture of normal cell lines is generally very difficult. Even for those that can be cultured, indefinite subculturing is impossible because of built-in senescence. Malignant cells, or hybrids of normal and malignant cells (e.g., hybridomas), overcome this built-in senescence and are said to be immortal.

Immunoadsorbent: An affinity matrix formed by linking an antibody preparation to an insoluble support.

Immunoaffinity chromatography: Purification of a compound (ligate) by using an affinity column in which the ligand is an antibody.

Immunoassay: Any assay method that uses antibodies for detecting and quantifying biological molecules (e.g., hormones or proteins) or microorganisms. The most commonly used methods are radioimmunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA). Many commercial immunoassay kits are available. Most of them are based on the use of monoclonal antibodies, which give much greater specificity than the use of polyvalent antisera.

Immunoblotting: The use of antibodies to detect a specific protein on a nitrocellulose sheet following protein (western) blotting (*see* Protein blotting). The nitrocellulose sheet is incubated in a solution containing an antibody (primary antibody) to the protein of interest. Following appropriate washing steps, the antigen–antibody reaction that occurs is thus visualized by incubating with a second antibody (anti-IgG), which binds to the primary antibody. The second antibody is used linked to a marker enzyme, usually horseradish peroxidase

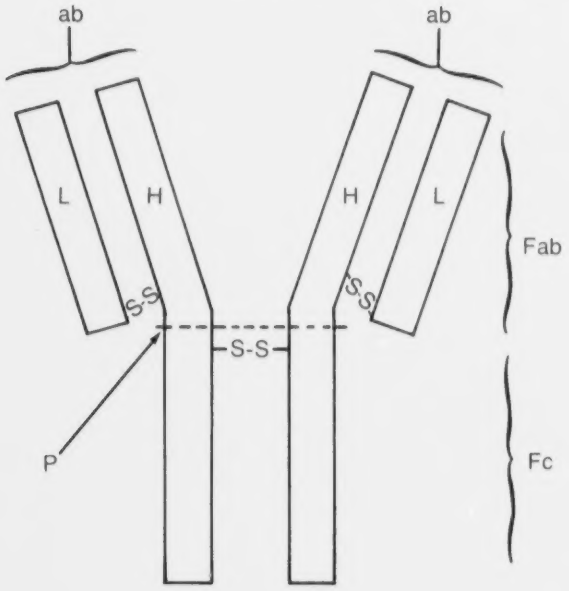
or alkaline phosphatase. After washing steps, incubation of the sheet in an appropriate chromogenic substrate solution for the enzyme results in the production of a colored band. The position of this colored band indicates the position of the protein of interest.

Immunogen: A substance used to induce an immune response.

Immunoglobulin: A class of globular protein that shows antibody activity. The five classes of human immunoglobulin are referred to as IgG, IgA, IgM, IgE, and IgD. *See also* Immunoglobulin G.

Immunoglobulin G (IgG): The major immunoglobulin component of serum. It makes up 75% of the total immunoglobulin content and has a MW of 160,000. The molecule comprises two light (L) chains and two heavy (H) chains that are held together by disulfide bridges. The molecule has two identical antigen-binding (ab) sites on what are termed the F_{ab} portions of the molecule. When the F_{ab} fragments are cleaved with papain they leave a crystallizable fragment (F_c), which is involved in complement fixation, macrophage fixation, and reactivity with rheumatoid factors. When an antigen (e.g., protein) is injected into an animal, a large number of different IgG molecules are

Immunoglobulin G



synthesized. Each one is capable of binding to a different epitope on the antigen (i.e., they differ in the structure of their F_{ab} region). *See also* Epitope, Antiserum.

Immunosensor: A biosensor in which an antibody is used to detect the molecule of interest. *See also* Biosensor.

Immunotoxin: A conjugate formed by linking an antibody to a toxin, such that both still retain their biological activity. Immunotoxins are being developed as a means of directing toxins (drugs) to target cells. For example, monoclonal antibodies against tumor-cell-surface antigens can be linked to toxic molecules. On injection into the patient the toxic molecule (drug) is directed to the tumor cell, where it exerts its toxic effect while leaving other tissues unaffected.

Impeller: *See* Agitator.

Inclusion bodies: *See* Protein inclusion bodies.

Incompatibility groups: *See* Compatibility.

Incubator: A controlled environmental system, room, or cabinet used to maintain microbial and cell cultures. It may involve the control of atmosphere, gas composition, humidity, light, and temperature.

Indoleacetic acid: *See* Auxins.

Induced mutation: *See* Mutation.

Induction: **(1) of λ phage**: Excision of integrated λ-DNA from the bacterial genome, leading to a change to the lytic mode of infection, caused by a chemical or other stimulus.

: **(2) of a gene**: Switching on of the expression of a gene or group of genes (operon) by a chemical (e.g., a hormone or substrate) or other stimulus (e.g., heat).

Inert support: Any nonreactive matrix. Inert supports are used for a range of purposes, including the immobilization of cells and enzymes, the growth of anchorage-dependent cells, immobilizing affinity groups for affinity chromatography, the attachment of a charged group to give an ion-exchange resin, and the solid-phase synthesis of peptides or oligonucleotides. A wide range of materials has been used, including glass, polymers, silica, and cellulose.

Infrared spectrophotometer: An instrument for the measurement of the adsorption of infrared radiation by a sample. Three major types are available: (1) dispersive, in which a prism or grating causes the radiation to be split into individual wavelength bands that are then scanned across the sample; (2) Fourier transform infrared (FTIR), in which the complete wavelength range is incident on the sample simultaneously, to give an overall spectrum of the sample; and (3) nondispersive, in which filters are used to select the appropriate wavelength required for analysis. The nondispersive type is used exclusively for quantitative measurement (e.g., on-line gas analyzer for carbon dioxide in the exhaust gas from a fermentor), whereas the other types may be used both qualitatively and quantitatively. The speed of FTIR, together with its powerful data analysis, allows it to be used as an on-line chromatographic detector.

Inherent kinetics: *See* Intrinsic kinetics.

In-line analysis: The analysis of a process by the use of direct-reading probes inserted directly into the process stream. This technique is to be preferred wherever possible, as it eliminates any errors caused by removing a sample from the process either by a continuous sample line or by a discrete sample, and it provides the facility for continuous monitoring of the process. Suitable probes are available for determinants such as temperature, pH, dissolved oxygen, pressure, impeller speed, and liquid and gas flow rates. *See also* On-line analysis, Off-line analysis.

Inoculum: The initial culture of an organism or mixed culture, added to a suitable medium to promote the propagation of a larger number of cells.

5′-Inosate (inosine monophosphate): A flavor enhancer produced commercially by the action of nuclease (5′-phosphodiesterase) from *Penicillium citrinum* and *Aspergillus* spp. on yeast RNA to produce the constituent ribonucleotides. In a second step, adenosine monophosphate is converted to inosine monophosphate by a 5′-AMP deaminase from *Aspergillus oryzae*.

λ Insertion vector: A λ phage vector produced by deleting a nonessential segment of DNA. This deleted region contains most of the genes involved in the integration and excision of the λ prophage from the bacterial genome. Such deleted vectors are consequently nonlysogenic and can exhibit only the lytic infection cycle. If a DNA mol-

ecule is inserted into the normal λ-DNA molecule, only about 3 kbp of DNA can be inserted before the DNA is too large to be packaged into the λ phage head. However, using a λ insertion vector, fragments of DNA ranging in size from 3 to 9 kbp can be cloned. *See also* Cosmid, λ Phage, Replacement vector.

Insertional inactivation: A cloning strategy in which insertion of a piece of DNA into a vector inactivates a gene carried by the vector. The loss of this gene product can be used to detect transformants (e.g., the loss of resistance to a particular antibiotic).

In situ hybridization: A technique for identifying the position of a gene on a chromosome. Cell preparations on glass slides are treated to denature their DNA (without losing the identity of the overall chromosome structures) and then washed with an appropriate radiolabeled probe. Hybridization occurs between the probe and the corresponding gene on the chromosome, and this hybridization can be detected by autoradiography.

Insulin: A polypeptide hormone that controls the level of blood sugar. About 20% of sufferers of *diabetes mellitus* are dependent on insulin injections to control their condition, and for over 50 years the hormone has been isolated from pig or cow pancreas. However, both sources of the hormone differ slightly in their amino acid sequence from human insulin. Consequently, nearly all patients develop circulating anti-insulin antibodies, which result in side effects and a need for increased dosage. The human insulin gene has now been cloned in *Escherichia coli* and was the first genetically engineered protein to be tested in humans. The use of this cloned material is now routine and, although it is too early to tell, it is anticipated that many of the side effects of animal-derived insulin will not occur with human insulin.

Integrative plasmids: *See* Episomes.

Intensifying screen: A solid layer of material (e.g., calcium tungstate) that fluoresces (emits visible light) when struck by β particles or X-rays. These screens are used to detect high-energy emissions, such as produced by ^{32}P or ^{125}I. These high-energy emissions pass straight through a photographic emulsion without being absorbed and therefore do not leave a latent image. When an intensifying screen is placed on the side of the film opposite to the source, the emitted energy is converted to light that forms a latent image on the film. Used in autoradiography.

Interferons: A family of proteins, originally identified as compounds produced by virally infected cells, that produce an antiviral state in other cells. They have been classified into three subtypes (α, β, and γ) with a number of proteins in each group. In addition to their antiviral effect, interferons inhibit cellular proliferation (hence are a potential anticancer drug) and modulate the immune system. These properties have made interferons much-sought-after compounds for clinical testing. Originally only prepared in small (and not very pure) quantities from human white blood cells, they are now being produced in quantity by at least three pharmaceutical companies that use recombinant DNA technology. This process provides sufficient material to carry out detailed clinical trials.

International unit of enzyme activity (IU): The amount of enzyme capable of producing 1 μmol of reaction product in 1 min under optimal (or defined) reaction conditions.

Intervening sequences: *See* Introns.

Intrinsic kinetics: Kinetics of an enzyme in free solution. For an immobilized enzyme, partitioning effects will affect the kinetic parameters obtained (still obeying Michaelis–Menten-type kinetics), and the kinetics are referred to as *inherent* kinetics. If diffusional limitations occur, the kinetics obtained are *effective* kinetics.

Introns: DNA sequences, found within the coding regions of most eukaryotic genes, that interrupt the code for the gene product. The full gene sequence is initially transcribed into hn RNA (heterogeneous nuclear RNA) and then the intron sequences are removed (cutting and splicing) to give the final mRNA molecule, which is then translated at the ribosome to give the protein product. The protein-encoding parts of the gene are referred to as *exons*. Bacterial genes do not contain introns and therefore do not possess the appropriate enzymes to remove these sequences. For this reason it is usually impossible to express a cloned eukaryotic gene in bacteria. A cDNA copy of the mammalian mRNA must be made first and then cloned into the bacterium. Sometimes referred to as intervening sequences.

Invertase: An enzyme that hydrolyzes sucrose into an equal mixture of glucose and fructose (invert sugar). The enzyme is isolated from *Saccharomyces cerevisiae* or *S. carlsbergensis*. Invert sugar, somewhat sweeter than sucrose, is mainly used in food and confectionary products as a humectant to hold moisture and prevent drying. Invert sugar is used in the preparation of artificial honey, by the brewing industry, in jam manufacture, and in making soft-centered chocolates.

Invert sugar: *See* Invertase.

In vitro: Literally, "in glass". Pertaining to a biological reaction taking place in an artificial apparatus, as distinct from observations made in living organisms (in vivo). *Compare with* In vivo.

In vitro mutagenesis: Any method that produces a mutation at a specific position in a DNA molecule. *See also* Site-directed mutagenesis.

In vitro packaging: The construction of infective λ bacteriophage particles that contain a DNA sequence to be cloned within the genome. Transfection of bacteria with λ DNA (containing the insert to be cloned) is highly inefficient. By packaging this recombinant molecule within an infective phage particle, the DNA can be introduced efficiently into bacterial cells. When the assembled virus is added to the bacterial culture, the normal λ phage infective process can take place.

In vitro protein synthesis: The addition of an mRNA sample to a cell-free translation system, usually in the presence of one or more radiolabeled amino acids, results in the translation of the mRNA molecule. The newly synthesized radiolabeled protein can be observed in a number of ways (e.g., gel electrophoresis followed by fluorography) to identify the protein coded for by the mRNA.

In vivo: Literally, "in life". Pertaining to a biological reaction that takes place in a living cell or organism. *Compare with* In vitro.

Ion exchange: A process in which adsorption of one or several ions on a surface is accompanied by a simultaneous desorption or displacement of an equivalent amount of another ionic species of the same charge. This often occurs on a surface of a polymeric molecular network that possesses functional groups capable of carrying an ionic charge. The counterions associated with these fixed charges are partially free and may exchange for other ions of the same charge in solution. The extent of this exchange depends on the nature and concentration of the exchanging ions. The material may be naturally occurring minerals (e.g., zeolites, aluminosilicates, or derivitized polymers of biological [dextran, cellulose] or synthetic [cross-linked polystyrene] origin).

Ion-exchange chromatography: A type of chromatography in which the solid support is an ion-exchange material used to separate mix-

tures of charged molecules or ions. This can be carried out on a preparative scale or as a modification of HPLC. *See also* Ion-exchange resin.

Ion-exchange fermentation: *See* Adsorption fermentation, of which this is a modification.

Ion-exchange resin: A synthetic organic polymer, often based on cross-linked polystyrene, that has been derivatized by the addition of charged groups to produce materials that will exchange counterions when suspended in aqueous solutions. Cationic exchangers have fixed acidic substituents based on, for example, sulfonic acid (SO_3H) (strong acid exchangers) or carboxylic acid (COOH) (weak acid exchangers). Anionic exchangers have fixed substituents based on, for example, quaternary ammonium (R_4N^+, Type I) or ethoxyamine ($-NH_2{}^+CH_2OH$, Type II) groups, or amines (R_3N), which are weak base exchangers. Other functional groups may also be attached to the resin skeleton to provide more selective behavior. These functional groups may be similar to those used in affinity chromatography. The degree of derivatization and the extent of cross-linking of the resin determines the overall capacity for ion exchange. *See also* Gel resin, Macroporous resin.

Ion-exclusion chromatography: The separation of electrolytes from nonelectrolytes by the use of an ion-exchange resin using the principle of Donnan membrane equilibrium. This principle requires that ions have a lower concentration within the pores of the resin or membrane than in the external solution. Nonelectrolytes are not affected by this principle and so the concentration within the pores will equal that of the external solution. Thus a partial separation of nonelectrolytes from electrolytes is possible. Under favorable conditions in a column, complete separation may be achieved.

Ionic strength: A function that allows the comparison of properties in solutions of different electrolytes (i.e., differing in ionic concentration or ionic charge). Ionic strength (I) is given by half of the summation of the molar concentration (C_i) of each of the ionic species in solution, multiplied by the square of their valences (z_i).

$$I = \frac{1}{2}\sum_i C_i z_i^2$$

Ion pair: Under certain conditions of high concentration or low di-

electric constant of the environment, ionic species of opposite charge may associate to form pairs that carry an effective zero charge.

$$A^+ + B^- = A^+B^-$$

Ion-pair partitioning: The separation and concentration of a charged species into an immiscible second phase by the formation of ion pairs. This can be achieved by selection of appropriate ionic species dissolved in the aqueous phase to form ion pairs, which can then partition between the two phases. More commonly, a compound will already exist as an ion pair in the organic phase (e.g., quaternary ammonium halides) and this solution is put in contact with the aqueous phase that contains the anion to be extracted. This anion will exchange with the halide ions from the quaternary ammonium compound and thus be extracted into the organic phase. Because ion pairs carry an effective zero charge, they can be present in a nonpolar organic solvent. Also called liquid ion-exchange or phase-transfer catalysis.

Ion-selective electrode: An electrochemical device that is sensitive to variations in activity (concentration) of a particular ion. Devices are commercially available for anions (e.g., halide or nitrate) and cations (e.g., ammonium, sodium, calcium). The electrodes may use either a solid-state membrane in the form of a crystal or pressed disk, or a liquid ion-exchange fluid contained by a porous polymer membrane as the sensor. All the devices suffer from interferences from similar ions and so are "ion selective" rather than "ion specific". They may be used as ion sensors in the monitoring of processes, but currently suffer from the disadvantage of not being steam sterilizable.

ISFET: Ion-selective field effect transistor, used as a sensor for monitoring a particular ion. *See also* Field effect transistor, ChemFET.

Isoglucose: *See* High-fructose syrups.

Isomerism: The ability of compounds having the same formula and molecular weight to possess different structural forms. Different types of isomerism are found; for example, structural (atoms are joined together in different arrangements) and stereoisomer (different arrangements in space of the same grouping). *See also cis* Isomers, *trans* Configuration, Dextrorotatory, Levorotatory, Chirality, Optical isomerism, Racemate.

Isomers: Compounds displaying isomerism.

Isopentenyladenine: *See* Cytokinins.

Isosbestic point: The defined wavelength(s) in the spectra of compounds in equilibrium at which the absorbance is constant and does not change as the relative concentrations of the compounds in equilibrium are varied. The presence of such isosbestic points may be taken to confirm the presence of such equilibria (for example, one isosbestic point infers the presence of two compounds in equilibria; two points, three compounds; etc.) The absence of an isosbestic point implies that the compounds in solution are not in equilibrium and that a process such as the one shown may be occurring:

$$A \rightleftharpoons B \rightarrow C$$

Isosbestic points are useful for quantitative analysis, as systems in equilibria obey the Beer–Lambert law only at these wavelengths. *See also* Beer–Lambert law.

Isoschisomere (isoschizomer): Two restriction enzymes that have the same target sequence are described as a pair of isoschizomers. For example, HpaII and MspI both recognize and cleave the following sequence:

5′ CCGG 3′
3′ GGCC 5′

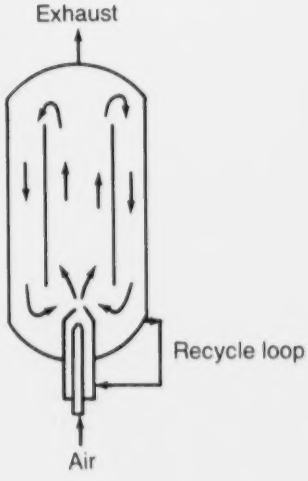
Isotonic solution: Solutions having the same osmotic pressure are said to be isotonic.

Itaconic acid: Methylenesuccinic acid. Produced industrially by the growth of *Aspergillus terreus* on either pure sugars or crude carbohydrates. Its major use is in the formation of polymers and in the synthesis of N-substituted pyrrolidones for use in detergents, shampoos, pharmaceuticals, and herbicides.

J

Jasmine oil: A compound isolated from plants of the *Jasminum* genus. Used in the cosmetics industry as a perfume.

Jet reactor: A type of fermentor in which the gas and feed solution enter at the base of the tank in such a way as to produce a jet of material that provides the energy required to agitate the contents of the tank. Used on the industrial scale for the production of yeast from whey.



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Karyotype: The chromosomal content of a cell. It can be abnormal in both overall quantity and the form of individual chromosomes. It is determined at the level of light microscopy.

kbp: Abbreviation for 1000 base pairs of DNA. Because of the considerable size of genomic DNA and fragments derived from such DNA, the size of DNA is not referred to by molecular weight, but more conveniently in terms of the number of kilobase pairs. Some authors abbreviate kbp to kb.

Keratin: A structural protein with a high sulfur content found in hair, feathers, horn, and shells of vertebrates. It is sometimes used as an adsorbent material for effluent treatment.

Kieselguhr: A form of diatomaceous earth. It is commonly used as a filter aid for filtering bacteria or gelatinous suspensions and has a voidage of approximately 0.85. *See also* Diatomaceous earth, Filter aid.

Kimal: A type of porous particulate aluminium oxide (alumina) used as a chromatographic support.

Kinases: Enzymes that catalyze the transfer of a phosphate group from ATP to another substrate. *See also* Polynucleotide kinase.

Kinematic viscosity: The ratio of the dynamic viscosity to density of a fluid measured at a constant temperature.

Kinetic viscosity: *See* Kinematic viscosity.

Kinetin (6-furfurylaminopurine): Probably the best-known cytokinin used in plant cell and tissue culture. It does not occur naturally in plants.

Kjeldahl nitrogen determination: A method of determining total nitrogen content of a substance by digesting with concentrated sulfuric acid in the presence of a catalyst and thereby converting the nitrogen to ammonia. The amount can be determined by titration, after the solution is made alkaline and the ammonia is distilled from the reaction mixture into an acid solution.

K_L: In aeration studies of a submerged liquid culture, K_L is the mass-transfer coefficient (cm dm^{-3}) and may be considered as the reciprocal of the resistances to the transfer of oxygen from the gas to the liquid phase. It is normally considered in a combined term, K_La.

K_La: In aeration studies, K_La is the volumetric transfer coefficient and is a measure of the aeration capacity of a fermentor, where *a* is defined as the gas–liquid interface area per liquid volume. It is extremely difficult to measure K_L and *a* separately, but the K_La can be determined by a sulfite oxidation technique, static gassing out, dynamic gassing out, or an oxygen balance technique.

Klenow fragment: Part of the *Escherichia coli* DNA polymerase I molecule, produced by the treatment of *E. coli* DNA polymerase I with subtilisin. The fragment still has the polymerase and 3′→5′ exonuclease activity, but lacks the 5′→3′ exonuclease activity of the original enzyme. It is used to "fill out" 5′ or 3′ overhangs at the ends of DNA molecules produced by restriction nucleases. In particular, this method is often used to radiolabel DNA molecules by using radiolabeled nucleotides. *See also* Nick translation.

Koji: A fungal proteolytic enzyme preparation produced by growing *Aspergillus oryzae* on a solid substrate such as rice or soybean. The enzyme is produced commercially for treating flour proteins and is used as a digestive aid called takadiastase.

Koji process: A traditional solid-substrate fermentation process for the fermentation of grain and soybeans by *Aspergillus* spp. The

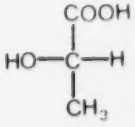
cooked substrate is inoculated with a pure culture and grown in shallow layers, where amylases and proteases are produced to break down the substrate and form Koji. This process forms the basis of a number of fermentations, including the production of organic acids (such as citric acid), rice wine (saké), and other sweetened rice fermentation products.

Label: A distinguishing feature or tag that can enable a particular molecule or group to be recognized. Labels can include isotopes, radioactive or heavy atoms, immune labels, antibodies or antigens, and colored or fluorescent dyes. *See also* Biotinylation, ELISA.

β-Lactamases: *See* Penicillinases.

Lactase (β-galactosidase)(E.C. 3.2.1.23): An enzyme (usually isolated from *Aspergillus niger*) that hydrolyzes lactose to glucose and galactose. Used industrially to convert waste whey (essentially a lactose solution) from the cheese industry to a sweeter solution of glucose and galactose that is of use to the confectionary and baking industry. Also used to hydrolyze lactose in skimmed milk and give a product suitable for consumption by people deficient in intestinal lactase who would otherwise experience unpleasant intestinal effects. It also helps to prevent the crystallization of lactose in ice cream.

Lactic acid: An organic acid with a range of industrial uses, especially as an acidulant and preservative in the food industry, where it is used as an additive to soft drinks, jams, syrups, and fruit juices. About half of the world's supply is produced industrially by the growth of *Lactobacillus* spp. on hydrolyzed starch or sugar solutions. Also produced on a small scale by the fermentation of lactose in whey by organisms such as *L. bulgaricus*.



Lactic acid bacteria: Gram-positive nonsporulating bacteria (rods or cocci) that produce lactic acid as a major or sole product of fermentative metabolism. The major genera are *Lactobacillus, Streptococcus, Leuconostoc,* and *Pediococcus. See also* Heterofermentative, Homofermentative.

Lactifers: *See* Latex.

Lactobacillus: A genus of Gram-positive, nonsporulating, rod-shaped bacteria. Most species are homofermentative, but some are heterofermentative. They are commonly found in decaying plant materials, milk, or milk products. *L. bulgaricus* is used for the preparation of yogurt, *L. acidophilus* for acidophilus milk, and other species in the production of cheeses, pickles, sauerkraut, and silage.

Lag phase: An initial period of time when growth does not occur, following the introduction of a microorganism into a nutrient medium that supports its growth. The lag phase may be considered as a period of adaptation to the new environment.

Lambda: Compounds beginning with λ are listed under their Roman names.

Lamellar settlers: Tanks (settlers) with plates or tubes (lamellae) inserted to increase settling efficiency by decreasing the distance a particle must settle and increasing the specific surface area of plates (lamellae). These lamellae are fixed at inclined angles so that cells or solids slide down and are collected. Particles that adhere to the lamellae can be removed by occasional vigorous agitation. Several types of settler are available.

Laminar flow: Movement of a fluid parallel to the walls of the container. Also known as streamline flow. In this regime of poor mixing the transfer of momentum, heat, or mass can occur only by diffusion. Converse of turbulent flow.

Langmuir adsorption isotherm: An isotherm that relates the amount of a species adsorbed (q) to that remaining in solution (c) at constant temperature. The Langmuir isotherm is applicable to a system in which the adsorbing surface is completely homogeneous and there is negligible interaction between the adsorbed species, such that the adsorbing species forms a monomolecular layer on the adsorbent. Thus

$$q = \frac{Qk_Lc}{1 + k_Lc}$$

where Q is the maximum adsorbed concentration and k_L is the equilibrium constant.

Laser Doppler anemometer: A noncontact optical device for the measurement of fluid velocity based on the scattering of laser light by small particles in the fluid. The shift of frequency that occurs as the result of the Doppler principle allows the velocity of the fluid to be calculated.

Latex: A milky emulsion of plant secondary metabolites (including terpenes, terpenoids, and alkaloids) that, on vulcanization, forms rubber. It is derived from a number of plant sources and produced in specific cells known as lactifers. Natural rubber is prepared from latex obtained from the plant *Hevea brasiliensis*.

Leachate: The solution that leaves a leaching operation. It consists of solvent that contains the leached material as solute.

Leaching: Removal of soluble components from an inert matrix by the percolation of a solvent to produce a soluble portion (leachate) and a residue, as, for example, in the extraction of sugar from sugar beet or oil from rape seed. *See also* Microbial leaching.

Lectins (phytohemagglutinins): Plant proteins with high affinity for specific sugar residues. They are useful for studying polysaccharides, glycoproteins, and cell membranes, and are also used in cell agglutination and cell typing. Certain lectins are used to induce mitogenic activity in tissue culture. *See also* Concanavalin A.

Legumes: *See Leguminosae.*

Leguminosae: One of the largest and most economically important families of flowering plants. One of the main reasons for their importance is their ability to fix atmospheric nitrogen in root nodules and to use the nitrogen compounds produced for growth (*see* Nitrogen fixation). Such crops therefore need little or no nitrogren fertilizer. Crops include soybeans, lentil, groundnut, and clovers (as animal fodder).

***Leptospirillum ferrooxidans* (*Ferrovibrio*)**: One of the organisms involved in bacterial leaching of minerals. It oxidizes iron or the iron moiety of pyrite, but not sulfur. *Compare with Thiobacillus ferrooxidans.*

Leuconostoc: A genus of Gram-positive nonsporulating bacteria that produce cocci in chains. They grow on fermentable carbohydrates

with the production of lactic acid, CO_2, and ethanol. In environments where sucrose is present, *L. mesenteroides* will produce dextran slimes, which can lead to blockage of pipes in sugar refineries. This dextran has also been used medically as a blood plasma extender.

Levorotatory: Description of the behavior of a chiral chemical such that in solution it rotates the plane of polarized light to the left. Denoted by the prefix L, as in L-dextrose. Converse of Dextrorotatory.

Ligand: A term used to describe a substance that interacts specifically and reversibly with a biological substance that is to be purified by affinity chromatography. The ligand (e.g., an enzyme cofactor, a triazine dye, a monoclonal antibody) is normally immobilized to a solid support.

Ligand-specific chromatography: *See* Affinity chromatography.

Ligases: Enzymes that join DNA molecules together. *See also* DNA ligase.

Ligate: The biological substance that is specifically bound by an immobilized affinity ligand.

Ligation: *See* DNA ligase.

Lignin: An abundant aromatic polymer found as a major component of lignocellulose. It is formed by the polymerization of monomers such as *p*-hydroxycinnamyl alcohols, where formation of a number of different bonds gives an irregular structure. These bonds are difficult to hydrolyze; thus lignin is highly resistant to microbial attack. Because of this resistance, lignin prevents access of microorganisms to the cellulose and hemicellulose components of lignocellulose. Straw, for example, is not extensively used as animal feed because very little of the cellulose polymer is accessible to the gut flora of the ruminants. The development of efficient delignification processes, both to increase availability of the plant biomass for microbial degradation and to degrade lignin to usable aromatic compounds, is therefore receiving considerable effort. Methods for lignin breakdown will offer new routes to many important aromatic intermediates central to the chemical industry. Unfortunately, only a limited range of microorganisms are known to degrade lignin. Both white-rot and soft-rot fungi can extensively degrade lignin, and brown-rot fungi and some bacteria can modify lignin. Of these, the white-rot fungus *Phanerochaete chrysosporium* shows considerable potential for industrial application to lignocellulose degradation.

Lignocellulose: All species of woods and woody plants (including straw and bagasse) contain three major components: cellulose, a collection of polysaccharides collectively known as hemicellulose, and lignin. These components are known collectively as lignocellulose. For example, softwood contains 40% cellulose, 28% hemicellulose, and 28% lignin. Lignocellulose, derived from the agriculture and forestry industries, is the most abundant source of biomass available to the biotechnological industries for the production of fermentable sugars and carbohydrates. However, because of its crystalline-ordered structure, the insoluble nature of the cellulose fibers, and the protective nature of the lignin sheath surrounding the cellulose fibers, lignocellulose is almost resistant to direct enzymatic attack. Expensive and energy-demanding pretreatments (e.g., grinding, acid treatment, steaming) of lignocellulose are therefore required to dissociate lignin from the polysaccharides and thus provide a substrate from lignocellulose that is suitable for microbial degradation. The development of methods for the direct microbial degradation of the lignin component of lignocellulose should help to overcome this problem in the future. *See also* Lignin.

Linkers: Short synthetic double-stranded polynucleotides containing one or more restriction endonuclease recognition sequences, used to attach sticky ends to a blunt-ended molecule. The linker is attached to blunt-end DNA by using T4 ligase and then cleaved by using the appropriate endonuclease to generate sticky ends. This DNA molecule can now be linked, by complementary base-pairing of sticky ends, to any other DNA fragment generated using the same restriction enzyme.

γ-Linoleic acid (GLA): 6,9,12-octadecatrienoic acid. A compound of importance to the pharmaceutical industry as a precursor in prostaglandin synthesis. It is currently produced from plant seeds (*Oenothera* sp. or *Boraginaceae*), but productivity is low because a long growth period and a huge area for harvesting seed are required. GLA is also produced by some fungi (e.g., *Mortierella* sp.), and production from this source is presently being investigated.

Lipases: Enzymes that hydrolyze triglycerides to free fatty acid, partial glycerides, and glycerol. Their natural substrates are triglycerides of long-chain fatty acids that are insoluble in water. Lipases, which are water soluble, hydrolyze the ester bonds at the interface between the aqueous phase and the insoluble substrate phase. Lipases are produced commercially from porcine and bovine pancreas and from microorganisms such as the yeast *Candida* and from *Aspergillus*, *Rhizopus*, and *Mucor* spp. Commercial applications of lipases include the hydrolysis of oils for soap manufacture, use as a digestive aid,

the promotion of interesterification of oils and fats, the formation of fatty acyl esters, to enhance flavor formation in certain cheeses, to manufacture cheese and butter flavors, and in detergents.

Lipophilic: A term used to denote the affinity of a substance for a nonpolar medium; converse of hydrophilic. Also called hydrophobic.

Lipophobic: A term used to describe the lack of affinity for nonpolar species; converse of lipophilic. Also called hydrophilic.

Liposomes: Small spheres whose walls are layers of phospholipid molecules. They are formed by mixing dry phospholipids (e.g., egg yolk or soybean lecithins) with water. As they form, liposomes entrap water and any water-soluble solutes that are present. Because of this entrapping ability, they are useful as drug-delivery systems.

Liquid chromatography: The separation and concentration of solutes by partition between a solid adsorbent and a mobile solvent phase. The adsorbent is normally in the form of a uniformly packed column to minimize diffusion effects. It produces a series of discrete bands that contain the separated components. Various adsorbents are used for particular types of separation (e.g., gel [molecular exclusion], affinity, adsorption, HPLC).

Liquid ion exchange: A term sometimes used to describe liquid–liquid extraction, in which the species being extracted from the aqueous phase undergoes an ion-exchange reaction transfer with ionic groups present in the organic phase as part of the organic extractant. An alternative term for ion-pair extraction and phase-transfer catalysis.

Liquid–liquid extraction: The partition of solutes between immiscible or partially miscible solvent phases. The partition may be assisted by the incorporation of molecules in either phase. Thus in an aqueous–organic system, ionic salts in the aqueous phase may increase the partition of an organic compound (salting out). Similarly, compounds in the organic phase may combine with an inorganic solute, increasing its partition into the organic phase by forming a nonpolar complex. *See also* Two-phase aqueous partitioning, Ion-pair partitioning, Liquid ion exchange.

Liquid shear: The relative parallel movement of elements in a fluid under an applied force. The application of liquid shear forms the basis of the principal mechanical method for cell breakage used in the large-scale disruption of microorganisms. A suspension of bacteria is forced through a small orifice under very high pressure. The sudden

drop in pressure on passing through the orifice causes the cells to expand rapidly and rupture. *See also* X-press.

Lithotroph: *See* Chemolithotroph.

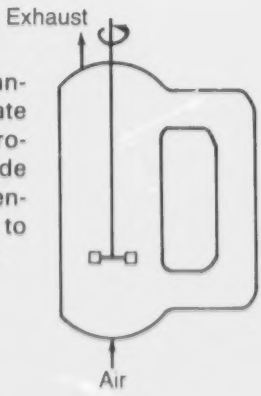
Load cell: A device for measuring the weight of a fermentor or for monitoring the feed rate from a small reservoir. The load cell is normally a solid or tubular steel cylinder, the compressive strain of which may be measured under axial load. Compressive strains over the appropriate range of loading are measured by means of electrical resistance strain gauges, which are cemented to the surface of the cylinder. Changes in resistance with strain are proportional to load. Load cells are available for a range of a few grams to thousands of tons. *See also* Strain gauge.

Loading: The level or concentration of a solute in a defined amount of solvent or support material in separation processes, such as liquid extraction or chromatography.

Log phase (exponential phase): The period of microbial growth when cells grow at a constant maximum rate. After the introduction of a microorganism into a nutrient medium that will support its growth, there is an initial lag phase followed by an interval during which the growth rate of the cells gradually increases (acceleration phase) until the cells grow at a constant maximum rate. This period is referred to as the log, or exponential, phase.

Long terminal repeats (LTR): Identical sequences of several hundred base pairs, introduced at each end of an integrated provirus during the synthesis and integration of viral DNA into a host cell genome during retrovirus infection.

Loop (recycle) reactor: A reactor that incorporates a recycle of the content (loop), together with additional makeup with the feed solution. One design incorporates an airlift to effect the recycle. This design has the advantages of no moving mechanical parts, a high rate of oxygen transfer, and a high volume of production. However, the disadvantages include problems with uniform mass transfer and an energy-intensive system with application limited to microbial systems. *See also* Airlift fermentor.



LTR: *See* Long terminal repeats.

Luciferin: *See* Bioluminescence.

Lumen: The central cavity of a tube, especially used in the context of capillaries and hollow fibers.

Lyophilization: The removal of water from a frozen sample by the application of vacuum. Also a drying method for long-term preservation of microbial cultures. A few drops of culture solution are placed in an ampoule and frozen in a dry-ice–ethanol mixture (–80 °C); then the plugged ampoule is attached to a vacuum source. Moisture evaporates under vacuum by sublimation. The evaporation maintains the frozen state of the sample until moisture evaporation is complete; the result is a preserved, dry pellet. The dried ampoule is sealed under vacuum and stored under refrigeration. Cultures are revived when required by adding a small volume of sterile water and streaking the suspension onto an agar medium. The method is also used to store protein samples in the solid state by lyophilization of aqueous protein solutions.

Lyotrophic series: *See* Hofmeister series.

Lysine: An amino acid, of considerable importance to industry as a feed and food supplement because it is an essential amino acid, found only in low levels in many cereals. It is produced industrially by the growth of *Brevibacterium lactofermentum* on glucose or *Corynebacterium glutamicum* on cane molasses. World production is 40,000 tons per year.

Lysis (of cells): The rupturing of membranes or cell walls (if present) in order to release the cell contents. The bacterial cell wall consists of a cytoplasmic membrane, surrounded by a rigid cell wall. Some species (e.g., *Escherichia coli*) have the cell wall surrounded by a second outer membrane. Lysis can be achieved by physical means such as mechanical force (*see* X-press, Liquid shear) or by chemical means such as lysozyme (which digests the cell wall), detergents such as sodium dodecyl sulfate (SDS) or isooctylphenoxypolyethoxyethanol (Triton X-100) (which remove lipid molecules, causing disruption of the cell membranes), or EDTA, which removes calcium ions that preserve the overall structure of the cell membrane. Often two or three of these are used together as a mixture.

Lysogen: *See* Lysogenic infection.

Lysogeny: *See* Lysogenic infection.

Lysogenic infection: A bacteriophage infection characterized by retention of the phage DNA molecule in the host bacterium for many thousands of cell divisions. For many lysogenic phages, the phage DNA is integrated into the host genomic DNA (*compare with* Lytic infection cycle). This integrated form of viral DNA is referred to as *prophage*. A bacterium carrying a prophage is physiologically indistinguishable from an uninfected cell. In this stable state the bacterium is referred to as a *lysogen* and is said to exhibit *lysogeny*. The integrated DNA is carried through many cell divisions, but eventually reverts to the lytic mode and lyses the cell. Both λ phage and M13 exhibit lysogenic infection and have been used as cloning vectors. Infection with λ phage involves integration into the genomic DNA, whereas M13 does not. *See also* M13.

Lysozyme: An enzyme produced commercially from hen egg white. The enzyme catalyzes the hydrolysis of β-1,4-glycosidic bonds in the mucopeptide of bacterial cell walls, and is therefore used as a method for lysing bacterial cells prior to product recovery. However, because of the cost, the enzyme is rarely used for large-scale extractions.

Lytic infection cycle: The series of events displayed by a bacteriophage that replicates and lyses the host cell immediately after the initial infection. The phage attaches to the bacterium and injects its DNA into the cell. The DNA both replicates in the cell and directs the synthesis of capsid proteins; the result is the formation of new phage particles that are released by cell lysis. At no stage is the viral DNA incorporated into the genomic DNA. *Compare with* Lysogenic infection.

M13: A filamentous lysogenic bacteriophage containing single-stranded DNA, used as a cloning vector, in particular to produce single-stranded DNA for sequence determination. Infection of *Escherichia coli* results in the continuous synthesis and release of new phage particles without cell lysis. Bacterial growth continues uninterrupted, although at a slower rate than normal. The genome of M13 is 6407 nucleotides long.

Mabs: An abbreviation for monoclonal antibodies.

Macerozyme: An enzyme preparation from *Rhizopus* spp., rich in pectinase, that is used to degrade plant cell walls and produce protoplasts.

Macrolide: Any high-molecular-weight molecule that is not a polymer of smaller subunits of similar chemical type. The term is used to describe a group of antibiotics (macrolide antibiotics) derived from various strains of *Streptomyces*. They all consist of a macrocyclic lactone ring (12-, 14- or 16-membered ring), to which novel amino or neutral sugars (e.g., erythromycin) are attached.

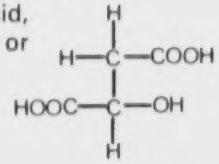
Macromolecule: A high-molecular-weight polymeric compound (e.g., protein, carbohydrate, nucleic acid).

Macroporous resin: A type of ion-exchange resin with an open porous structure capable of adsorbing large ions. These resins have better kinetics for large molecules than gel resins, but they have a lower overall capacity. Because of the open pore structure, macroporous resins also have better resistance to osmotic shock than the gel type. Also termed macrorecticular resins. *Compare with* Gel resin.

Macrorecticular resin: *See* Macroporous resin.

Magnetic separation techniques: The use of magnetic solids to enhance the separation of substances by the application of an external magnetic field. Enzymes immobilized on a magnetic solid can readily be separated from other particulate matter by the application of a magnetic field (i.e., a magnetic filter). The opposite effect can be generated, so that an enzyme attached in this way can be fluidized or stirred magnetically. Similar systems can be designed by attaching species to micromagnetic substances for affinity chromatography, ion exchange, immunoassay, etc. *See also* Diamagnetism, Ferromagnetism, Paramagnetism.

Malic acid: A compound used as an acidifying agent in the food industry. It is produced from fumaric acid, either by fermentation with *Paracolobactrum* sp. or with immobilized fumarase.

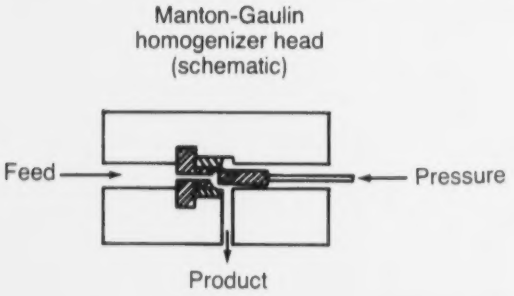


Malt: A term used to describe barley grains that have been steeped in water, drained, allowed to germinate, and dried at defined temperatures in a kiln. During this process the starch and proteins in the grain are partially degraded. The kilning ensures that about 70% of the original dry weight will be available as soluble components such as dextrins, sugars, and proteins when mashed during wort preparation in a brewery.

Mammalian cell culture: *See* Animal cell culture.

Manometry: A technique for measuring changes in gas pressure that result from the uptake or release of gases as a consequence of chemical or biological action, as in the Gilson respirometer or Warburg manometer.

Manton–Gaulin–APV homogenizer: A device for the disruption of cells. The cells are forced through a small orifice onto an impact ring.



Mass balance: The analysis of a process in which the mass of reactants is correlated with the mass of products according to the law of conservation of mass. That is,

$$[A] + [B] = [C] + [D]$$

Mass flow sensor: A type of sensor used for the measurement of fluid flows. Three commercially available types are designed on two main principles.

: **(1)** A true mass flowmeter, an example of which is the axial flow–transverse momentum mass flowmeter. This instrument uses the axial flow through a driven impeller and turbine in series. The impeller imparts angular momentum to the fluid. The fluid momentum causes a torque to be imparted to the turbine, which is restrained from turning by a spring. The measured torque is proportional to the rotational speed of the impeller and the mass flow rate of the fluid.

: **(2)** An inferential mass flowmeter. In this case a head meter (e.g., orifice or venturi) is used in conjunction with a densitometer. The signal from the head meter is proportional to ρV^2, where V is fluid velocity. Compensation for the density, ρ, gives V proportional to the mass flow.

: **(3)** The latest device uses the scatter of ultrasonic radiation by the fluid and thus provides a sensor that has no contact with the fluid being measured.

Mass spectrometer: An instrument in which a molecule is fragmented into charged species of varying mass-to-charge (m/e) ratio by the application of high-energy electrons in a vacuum. Alternative meth-

ods for molecular fragmentation exist [e.g., chemical ionization (CI) and fast-atom bombardment (FAB)]. The resulting charged species are separated by a combination of electric and magnetic fields according to their *m/e* ratios, and are then detected and displayed as a plot of abundance versus *m/e*. This device aids in clarification of structures of complex molecules. It also serves as a powerful and versatile detector for chromatography and as an on-line monitor for evolved gases and volatile products.

Mass transfer: The transfer of a given component in a system across space under the influence of driving forces such as concentration differences and temperature variation. This process may occur within a single phase (e.g., diffusion) or across boundaries (e.g., membranes). The term is used to describe the exchange of materials between the surface of an organism and its external environment (i.e., the uptake of nutrients and the elimination of waste metabolites).

Mass-transfer coefficient: A quantity that characterizes the extent of mass transfer within a system or across a boundary, defined as the ratio of mass flux to the difference between mass fractions on either side of the boundary. The mass-transfer coefficient can be correlated with the Reynold (Re) and Schmidt (Sc) numbers in forced convection systems as:

$$Sh = a\,Re^{b}\,Sc^{c}$$

where Sh is the Sherwood number and the coefficients *a, b,* and *c* are normally determined experimentally. However, predictions can be made in a number of flow regimes, such as laminar flow:

$$Sh = 0.664\,Re^{1/2}\,Sc^{1/3}$$

For oxygen gas transfer:

$$Sh = 0.13\,Re^{1/4}\,Sc^{1/3}$$

For natural convective systems the Grashof number, Gr, replaces the Reynolds number; thus:

$$Sh = a'Gr^{b'}\,Sc^{c'}$$

See also Grashof number, Reynolds number, Schmidt number.

Mastigomycotina: A subdivision of the fungi, which has hyphae without cross walls. The sexual organs are the antheridium (male) and the oogonium (female). Fusion leads to the formation of oospores within oogonia. Many also asexually produce sporangia that contain zoospores (motile). Many fungi in this group are plant pathogens that cause blights and damping off, but none are used industrially.

Maxam–Gilbert method: A chemical method for sequencing DNA. The radiolabeled DNA sample to be sequenced is divided into four aliquots. Each aliquot is chemically treated to cause random cleavage at one of the four nucleotides. The fragments generated from each reaction are separated in adjacent lanes on a polyacrylamide gel, and the DNA sequence is read directly by examination of the gel pattern obtained by autoradiography.

Maxicells: *Escherichia coli* cells that contain mainly plasmids, with very little chromosomal DNA. When certain *E. coli* cells are irradiated with UV light, chromosomal DNA is extensively degraded, but multicopy plasmids within the cell are relatively undamaged. Such plasmids continue to replicate after irradiation. This replication produces cells that contain mostly plasmid DNA and synthesize plasmid gene products almost exclusively. Such systems are ideal for studying plasmid-encoded products. *See also* Minicells.

Maximum oxygen-transfer rate: The product of volumetric mass-transfer coefficient and oxygen solubility in the medium used to evaluate oxygen-transfer rate capacity of a fermentor. It may be determined by the sulfite method, whereby sulfite ions are oxidized to sulfate by oxygen in the presence of copper ions as a catalyst. The residual sulfite concentration is determined by titration with iodine. Alternative methods of determination include the use of dissolved oxygen probes to measure the dynamic oxygen balance in the fermentor and the monitoring of the oxygen balance between the inlet and exhaust gas streams.

Mediated membrane transport: *See* Facilitated membrane transport.

Medium: A solid or liquid substrate that will support the growth of an organism. All organisms require water, sources of energy, carbon, nitrogen, mineral elements, possibly vitamins, and oxygen if aerobic. The medium may consist of pure compounds (defined medium) or crude animal or plant extracts (complex medium). Media may be specially devised for isolation, sporulation, inoculation, or product formation.

Medium-pressure liquid chromatography: A form of partition chromatography involving a solid matrix and a liquid mobile phase, operating under lower pressures (~40 bar) than normally experienced with HPLC. This pressure level allows the use of glass columns. It may be used on a large scale with liquid flow rates of 3–160 cm^3/min for separations of proteins, etc.

Meiosis: A form of cell division in which half the normal complement of chromosomes is generated in each of the daughter cells. These daughter cells are haploid, whereas the original cell is diploid.

Melting (of DNA): The separation of a DNA molecule into its component chains (denaturation) by heating a solution of the DNA. Hydrogen bonds are disrupted by the heating process. Most DNA samples begin to melt at about 70–80 °C; they are usually completely melted at 95 °C. The midpoint of the temperature range over which the strands of DNA separate is called the melting temperature, denoted T_m.

Melting temperature (of DNA) (T_m): *See* Melting.

Membrane: An insoluble porous layer or film of material forming a division between two fluids, across which molecules or ions may be transported. Membrane pores of a defined size can be used in processing for microfiltration, ultrafiltration, reverse osmosis, dialysis, etc. Various configurations of membrane equipment are possible, including flat sheets; leaf or plate, where the membrane is cast directly onto the support; spiral wound, consisting of a sandwich of porous sheets and spacers wound into tubes; wide-bore tubes, 10–25-mm i.d.; narrow-bore tubes, 2–10-mm i.d.; and hollow fibers, 1–2-mm i.d. Two types of synthetic membrane are available, anisotropic (asymmetric) and homogeneous (amorphous). The former are membranes with a thin dense layer (0.1–10 μm thick) supported by a much thicker (2–5-mm) spongy porous substrate. The thin dense layer achieves the required separation with little resistance to permeation because of its thinness, while the backing support provides strength. The very open structure allows rapid transport to the permeate, again with little resistance. Homogeneous membranes, as their name suggests, have the same structure throughout their thickness.

Membrane distillation: A technique whereby a substance is distilled through a membrane as a result of a temperature difference across the membrane. The pores of the membrane are filled with vapor of the substance being transferred, and it is bounded by two liquid phases. *Compare with* Pervaporation.

Membrane filtration: A number of processes in which a polymeric membrane acts as a barrier through which a fluid permeates. The pore size and construction of the membrane allow different-sized particles to be retained and thereby acts as a separation process. *See also* Dialysis, Microfiltration, Reverse osmosis, Ultrafiltration.

Membrane reactor: Either a type of fermentor in which a membrane separates the feed and product streams or one in which a biocatalyst is immobilized on the membrane. Two main designs are used.

: **(1)** The membrane separation unit is on-line with a reactor, and the reactor contents are pumped continuously through the separator. The permeate, containing the products, is removed while the retentate, containing the biocatalyst and nutrients, is returned to the reactor. The membrane separation processes that may be involved include micro- or ultrafiltration and pervaporation.

: **(2)** The biocatalyst is immobilized within the membrane. Either a pressure difference drives nutrients and products across the membrane, or the module is diffusion-controlled so that nutrients and products occur on both sides of the membrane. *See also* Dialysis fermentor.

Membrane separation processes: The use of a membrane to assist in separation of reactants and products. This technique can separate mixtures with similar chemical and physical properties, as well as isomers and thermally unstable compounds. The processes can be used by themselves or in conjunction with conventional separation processes. *See also* Dialysis, Electrodialysis, Microfiltration, Pervaporation, Ultrafiltration.

Meristem: Concentrated regions of active cell division in plants, where most coordinated cell division takes place and from which permanent tissue cultures can be derived (e.g., tips of stems and roots; apical meristems).

Merrifield synthesis: This term generally refers to the solid-phase synthesis of peptides, a procedure originally pioneered by Merrifield and his co-workers.

Messenger RNA: An RNA molecule synthesized from a DNA template by the enzyme RNA polymerase. The mRNA sequence is complementary to (i.e., base-pairs) the DNA sequence.

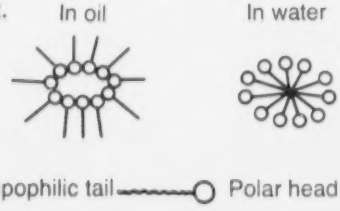
Metalloprotease: One of the four categories of classification of proteases; the others are serine, thiol, and carboxyl proteases. All metalloproteases have a metal ion involved in the catalytic mechanism and are therefore inhibited by chelating agents such as EDTA.

Methanogen: A methane-producing strain of bacteria. This group includes the following genera: *Methanobacterium, Methanococcus, Methanosarcina.*

Methylotroph: An organism that can grow on organic compounds that contain no carbon–carbon bonds. The genera include *Methylomonas* and *Methylococcus,* which use methane, methanol, or formaldehyde as their sole carbon and energy sources.

MIC: *See* Minimum inhibitory concentration.

Micelle: A colloid formed by the reversible accumulation of molecules above a critical concentration (cmc) in a solvent. Charged molecules form colloidal electrolytes such as soaps or detergents, in which the charged groups aggregate with water molecules. *See also* Critical micelle concentration (cmc).



Micellular enhanced ultrafiltration: A technique used mainly in the purification of wastewaters for the separation of substances normally too small to be removed by ultrafiltration. The process involves the adsorption of the impurities into micelles formed by surfactants. This adsorption increases the particulate size and enables ultrafiltration to be used successfully. Cationic surfactants are used to form micelles for nonionic organic materials, and anionic surfactants are used for metallic impurities.

Mickle tissue disintegrator: *See* Bead mill.

Microbial leaching: The use of microorganisms to solubilize metals in industrial extraction processes. The extraction of metals from insoluble minerals (mainly mineral sulfides) is achieved through leaching by acidophilic iron-oxidizing and sulfur-oxidizing bacteria. This solubilization of metals from their ores produces concentrated solutions of metals that can be recovered with hydrometallurgical processes. Although a number of microorganisms are involved in these

processes, the principal acid-generating microorganism affiliated with the microbial degradation of sulfide mineral is *Thiobacillus ferrooxidans*. This organism oxidizes ferrous iron and reduced-oxidation-state sulfur compounds. At present the process is largely confined to the copper and uranium industries.

Microcarrier: A small beaded matrix (≈100–200-μm diameter) used as a support for the culture of anchorage-dependent cells. Beads can be of silica, glass, collagen, DEAE-Sephadex, polyacrylamide, etc. Cells grown in this way can be treated as a suspension-cell culture, and fermentation technology processes for suspension culture can be used.

***Micrococcus luteus* polymerase**: A DNA polymerase that also has 5′ to 3′ exonuclease activity. It is used to create small single-stranded regions in cloned DNA molecules starting from a nick.

Microencapsulation: The encapsulation of enzymes within spherical semipermeable polymeric membranes. This method is commonly used as an enzyme immobilization method, but is also used as a drug-delivery system. The membrane material is chosen such that large molecules (e.g., enzymes) are retained within the sphere (artificial cell), although substrate and product molecules can freely diffuse across the membrane. Membrane materials that have been used successfully include cellulose nitrate, nylon, gelatin, silicone rubber, polyurethanes, epoxy resins, and polyamides. *See also* Liposomes.

Microfiltration: A process for the membrane-filtration removal of particles in the 0.1–10-μm range. The technique can be used in either a cross-flow (tangential) or static dead-end configuration. The separation is characterized by the pore size of the symmetrical microporous polymer membrane and the particle size of the impurities. Two levels of particulate removal are generally considered: nominal rating (90–93% removal) and absolute rating (100% removal). The driving force for the process is a pressure difference across the membrane, normally of the order $1–5 \times 10^5$ Pa. The technique may be used for sterile filtration, clarification, cell harvesting, and bacteria or virus separation. *See also* Crossflow filtration, Dead-end filtration.

Microfluorimeter: A device for automatically counting cells by means of the fluorescence that results from passing a suitably stained cell through a laser beam. The device can be modified to determine components in the biomass by selective staining (e.g., proteins or nucleic acids). In addition, the use of multiple lasers and optical processing

of the fluorescence signal will allow more than one stained species to be counted simultaneously. *See also* Flow cytometry.

Microinjection: A method for introducing DNA into a cell by injecting it directly into the cell nucleus with an extremely fine syringe needle, usually a glass micropipet that has been drawn out to a diameter of 0.1–0.5 μm.

Microplasts: Small vesicles produced by the fragmentation and subdivision of protoplasts. They contain small amounts of the original genetic material from the parent protoplast and can be fused with a complete protoplast. This fusion introduces new genetic information into the protoplast. It is the equivalent of the use of minicells to transform bacterial cells.

Micropropagation: The clonal propagation of plants in vitro.

Microtiter plate: Plastic plates (polystyrene, polypropylene, or polyvinyl) consisting of eight rows of 12 flat-bottomed wells, each with a volume of about 400 μL. Used in particular for ELISA assays, in which antigen or antibody is adsorbed onto the surface of each well and all antigen–antibody reactions take place in solution inside the well.

Mineral leaching: *See* Microbial leaching.

Minicells: Small nongrowing bodies produced by aberrant cell division at the polar ends of bacteria. They do not contain chromosomal DNA. The introduction of a plasmid, cloned DNA, or phage genome into a minicell results in RNA and protein synthesis, which can be analyzed in the absence of host cell products because genomic DNA is absent. Minicells are particularly useful for analyzing plasmid-encoded gene products. *See also* Maxicells.

Minimal medium: A defined medium that provides only the minimum number of different nutrients needed for the growth of a particular microorganism.

Minimum inhibitory concentration (MIC): The lowest concentration of an antibiotic or similar compound in a dilution series of broth tubes that shows no growth of the test organism (e.g., *Staphylococcus aureus*) after incubation for a standard time and temperature. Standard-sized drops of 24-h cultures are used as inocula.

Miscibility: The ability of two substances to form a single phase at all relative concentrations. *See also* Partially miscible substances, Immiscibility.

Mismatching: Regions in a double-stranded DNA molecule or DNA–RNA hybrid, where the bases on the respective strands are noncomplementary and therefore do not hydrogen bond.

Mitosis: The common form of cellular division, in which the normal complement of chromosomes is generated in each of the daughter cells.

Mitotic index: The percentage of a total cell population of a culture that, at a given time, exhibits some stage of mitosis.

Mobile phase: In chromatography, the carrier phase (liquid or gas) that moves relative to the stationary phase (support) to bring about partition and separation.

Mobilization (*mob*) genes: Genes involved in the transfer of a plasmid from one cell to another. If a plasmid that has had its transfer (*tra*) genes deleted is present in a cell with a plasmid that does have *tra* genes, then this plasmid is capable of being transferred to another cell (*see* Transfer genes) as long as it contains the so-called mobilization (*mob*) genes. The plasmid is said to be mobilized. Laboratory-used plasmids therefore have their *mob* genes (as well as their *tra* genes) deleted to prevent the possibility of mobilization of recombinant plasmids if they should escape from the laboratory environment.

Modified field effect transistor (MOSFET): *See* Field effect transistor.

Molasses: The residue remaining after the repeated crystallization of sugar extracted from sugar cane or sugar beet. It contains sucrose; glucose; fructose; and, if from beet, raffinose and some dextrans.

Molecular diffusivity: The rate of diffusion of a molecule (diffusivity). Because diffusivity depends on the physical state of the surrounding fluid, diffusivities in gases are about 10^4 times greater than in liquids. Diffusivities can be estimated on the basis of the kinetic theory, which is much better developed for gases than for liquids.

Molecular distillation: A distillation process carried out under very low pressures (1.3 N/m^2 or less) in equipment with a short distance

between the surface of the liquid and the condensing surface. Because the mean free path of the molecules in the vapor is the same order of magnitude as the distance to the condensing surface, rapid distillation is possible and thermal decomposition is minimized. The technique can be used for the final concentration of vitamins and natural products as an alternative to freeze-drying.

Molecular exclusion chromatography: *See* Gel filtration.

Molecular sieve: An inert material, often an aluminosilicate, available in a range of defined pore sizes for the separation of molecules or compounds. Especially useful for the separation of gas mixtures and the removal of water from gases or organic solvents.

Monoclonal antibody: An immunoglobulin produced by a single clone of lymphocytes. A monoclonal antibody recognizes only a single epitope on an antigen and therefore cannot precipitate antigens by forming a cross-linked three-dimensional precipitation matrix, as is the case with a polyclonal antiserum. In the laboratory, monoclonal antibodies are produced from hybridoma cells. *See also* Hybridoma cell.

Monod kinetics: A kinetic expression for the growth rate of microbial species:

$$\mu = \frac{\mu(\max)[S]}{K_s + [S]}$$

where μ is specific growth rate; $\mu(\max)$ is maximum specific growth rate; K_s is saturation constant (Monod coefficient); and $[S]$ is substrate concentration.

Monolayer: A single layer of adsorbed molecules on a support or at a fluid interface; a one-molecule-thick film.

Monolayer culture: A single layer of cells on the surface of a culture vessel. Most cultures of mammalian cells grow by attachment to a glass or plastic surface (anchorage dependence). This attachment forms a monolayer.

Monomer: The repeat unit in a polymeric structure; the simplest molecule capable of producing that polymer.

Monosodium glutamate (MSG): A compound much used as a flavor enhancer in the food industry. It is produced by fermentation of *Co-*

rynebacterium or *Brevibacterium* spp. World production exceeds 100,000 tons per year. *See also* Glutamic acid.

Montmorillonite: A clay mineral (aluminosilicate) with variable composition and pronounced adsorptive properties, which may be used as a filter aid or adsorbent.

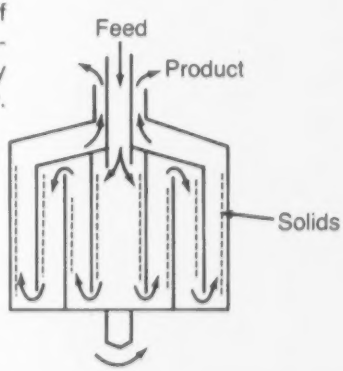
MOSFET: Abbreviation for modified field effect transistor. *See also* Field effect transistor.

mRNA: *See* Messenger RNA.

mtDNA: DNA found in mitochondria (mt). Also mitDNA.

Mucor: A fungal genus classified in the *Zygomycotina*, which are widespread in soil and often cause storage rots and other spoilage problems in materials contaminated with soil. *M. lacemosus* can be grown in submerged culture to produce ethanol.

Multichamber centrifuge: A modification of a tubular bowl centrifuge in which the bowl consists of a series of concentric tubular sections of increasing diameter that form a continuously enlarging passage for the liquid flow. The feed is introduced into the center of the bowl and hence into the smallest-diameter tube, where it experiences the least centrifugal force. From the center it passes by channels into chambers of increasing diameter, and hence increasing centrifugal force. The heavier particles are deposited in the smaller chambers and the lighter particles in chambers with a larger diameter. The total holding volume for solids is not improved by sectioning the bowl into chambers, but separation of the particles by size improves the clarification of the emerging liquid. The largest devices are used in the clarification of fruit juices, beer, etc.



Multidentate ligand: *See* Polydentate ligand.

Murine: Pertaining to mice.

Mutation: A chemical change in the DNA of an organism leading to a change in the genetic character. The DNA change is inherited unless

the mutation is lethal. A strain exhibiting such a changed characteristic is termed a mutant. Each time a microbial cell divides there is a small probability of an inheritable change occurring (spontaneous mutation). However, mutations are often deliberately introduced (induced) into organisms in an attempt to produce an improved strain. Mutations can be achieved by the use of UV radiation, ionizing radiation, or chemicals (e.g., nitrous acid).

Mycelium: The collective term for a network of hyphae.

Mycoplasmas: The smallest living cells known. They are generally spherical, with a diameter varying from 0.3 to 0.8 μm. However, filamentous forms also exist, with diameters of 0.1 to 0.3 μm and lengths of up to 150 μm. A solution that has been "sterilized" by filtration through a 0.2-μm filter can therefore still contain mycoplasmas. Up to 15% of all cell cultures in the world are contaminated by mycoplasmas, many of which exist symbiotically with growing cells. Bovine mycoplasmas (45%), human oral species (33%), and porcine mycoplasmas (21%) are the main contaminating species. The elimination of mycoplasmal contamination from biotechnological products like monoclonal antibodies and viral vaccines is a major problem, but antibiotics such as BM cycline are proving successful in eliminating the problem.

Mycoprotein: A food product (single-cell protein) consisting of fungal mycelium, produced by Rank Hovis MacDougall for human consumption. The organism used is a strain of *Fusarium graminearum*. The mycoprotein protein production process involves continuous fermentation with glucose as substrate and ammonia and ammonium salts as nitrogen sources. Following fermentation, the culture is heat-treated to reduce the RNA content. The mycelium is separated by vacuum filtration.

Mycorrhiza: An association of a nonpathogenic fungus with the root of a plant. In ectomycorrhiza, caused by basidiomycete and ascomycete fungi, the fungi proliferate to form a sheath around the fine roots. In endomycorrhiza, the fungi invade root cortical tissues. A form of endomycorrhiza known as vesicular–arbuscular (VA) mycorrhiza has particular agricultural importance. *See also* Vesicular–arbuscular mycorrhiza.

Mycotoxin: Any low-molecular-weight fungal secondary metabolite capable of producing toxic effects in humans or animals. They are

produced most commonly on grains and nuts stored in humid conditions. *Aspergillus flavus* produces a series of aflatoxins that are extremely toxic. These toxins are heat-stable and normally withstand food-preparation temperatures.

Myeloma cell: An immortalized (malignant) antibody-secreting tumor cell derived from a B-lymphocyte. *See also* Hybridoma cells.

Nabla factor: *See* Del factor.

National Laboratory Gene Library Project: A project aimed at providing chromosome-specific human gene libraries for the scientific community. Separate HindIII and *Eco*RI digests of individual chromosomes, isolated by flow cytometry and sorting, have been cloned in the bacteriophage vector Charon 21A. Average insert size is 4 kbp. The construction of libraries with larger inserts (20–40 kbp), by using either the lambda vector Charon 35 or the cosmid vector Homer 4, are planned.

Natural-circulation evaporator: An evaporator in which the circulation is provided by natural convection that is induced by vapor formation in the heat-exchanger tubes contained in the feed vessel. Circulation is normally via a central downcomer through the heat exchanger.

Necrotrophic fungi: Fungi that obtain nutrients from dead host cells.

Nephelometry: The quantitative assessment of a suspension of particles by the measurement of scattered light at right angles to the incident beam. The technique, more sensitive than turbidity measurements, can be used at lower particle concentrations and with smaller particles, but it requires more precise optics. The angular

dependence of the amount of scattered light is a characteristic of a microorganism and can be used to identify species under favorable conditions.

Nernst equation: A thermodynamic equation that relates the observed electrode or redox potential to the conditions in a system. The form of the equation is

$$E = E^o + \frac{RT}{nF} \ln \frac{[\text{oxidized form}]}{[\text{reduced form}]}$$

where E is observed potential; E^o is standard potential; R is the gas constant; T is absolute temperature; n is number of electrons involved in the system; F is the Faraday constant; and [ ] denotes concentration or activity of the species involved.

Nernst layer (Nernst–Planck layer): A thin layer of unstirred solvent that surrounds a particle in a stirred solution. The thickness of this layer is affected to a large part by the rate at which the solution is stirred. This layer causes diffusional limitations for immobilized enzymes by restricting the rate of substrate diffusion to the enzyme.

Neutrase: A protease from *Bacillus subtilis* added to cheeses prior to the ripening stage to reduce maturation time.

Newtonian fluid: A fluid that has a constant viscosity that is not influenced by the shear rate. The viscosity of a Newtonian fermentation broth will not vary with changes in the agitation rate.

Nick: A region in a double-stranded DNA molecule in which the phosphodiester bond is broken on one of the polynucleotide chains.

Nick translation: An enzymatic method of radiolabeling a DNA molecule. Free 3′-hydroxyl groups are first formed randomly within the unlabeled DNA ("nicks") by using a nuclease such as pancreatic deoxyribonuclease. DNA polymerase I is then added with one or more radiolabeled nucleotides. As well as being a polymerase (it adds a nucleotide to a free 3′-OH group), this enzyme also possesses 5′ to 3′ exonuclease activity. As the enzyme removes nucleotides (starting at the "nick"), in the 5′ to 3′ direction, it replaces a radioactive nucleotide by adding it to the free 3′ hydroxyl group at the "nick". In this way the "nick" is shifted along (translated), one nucleotide at a time. The removed nucleotide is replaced by a radioactive one. By means of this "hot for cold swap" of nucleotides, about 50% of the residues in the DNA can be radiolabeled.

Nitrification: The microbial conversion of ammonia to nitrate ions. Two major genera are involved in this overall conversion process: *Nitrosomonas,* which convert ammonia directly to nitrate, and *Nitrobacter,* which convert nitrite to nitrate.

Nitrilotriacetic acid (NTA): A synthetic, metal-complexing organic chemical extensively used to replace polyphosphates in washing powders. Both NTA and polyphosphates are used to sequester calcium ions and thus enhance frothing, but NTA has the advantage that it is biodegradable.

Nitrogen fixation: The conversion of atmospheric nitrogen into an organic form. It can be carried out by bacteria and blue-green algae. Commercially, the most important process occurs in the roots of leguminous plants. *Rhizobium* bacteria invade the roots of the plants and form root nodules, where nitrogen fixation takes place. The plant is able to use the nitrogenous compounds produced. The relationship between the bacteria and plant is symbiotic. The transfer of nitrogen-fixing genes into crop plants is one of the major aims of plant molecular biology, although it may turn out to be easier and as effective to induce symbiosis between *Rhizobium* and nonleguminous crop plants. *See also* Symbiosis, *Rhizobium, Azotobacter.*

Nonidet P-40: A nonionic detergent (an octylphenol–ethylene oxide condensate averaging 9 mol of ethylene oxide per mol of phenol). Often used to solubilize proteins and to minimize nonspecific hydrophobic interactions in techniques such as ELISA and protein blotting.

Noninvasive sensors: Sensors that can monitor a change in a parameter without being in direct contact with the medium (e.g., γ-ray level detectors, ultrasonic flowmeters).

Nonionic surfactant: A detergent molecule that is uncharged in solution. These compounds usually consist of condensation products of alcohols or phenols with ethylene oxide, for example, Nonidet P-40. *See also* Anionic surfactant, Cationic surfactant.

Non-Newtonian fluid: A fluid that does not follow Newtonian fluid behavior. The viscosity of a non-Newtonian liquid will vary with the shear rate (i.e., the viscosity will vary with the agitation rate). Broths with polysaccharides or mycelial cells display non-Newtonian rheology. Several types of non-Newtonian liquid are recognized (e.g., Bingham plastic, Casson body, Dilatant, and Pseudoplastic).

Nopaline: *See* Opines.

Northern blotting: The transfer (either by diffusion or electrophoretic transfer) of separated RNA molecules from a gel medium (e.g., agarose) to a nitrocellulose or nylon sheet where the RNA binds. The separated RNA molecules can then be further investigated (e.g., by washing the support in an appropriate probe solution). The method is analogous to Southern blotting for DNA.

NTA: *See* Nitrilotriacetic acid.

Nuclear polyhedrosis virus: A virus used in an insecticidal spray for the control of a sawfly *Neoprion sertifer* in coniferous forests. The active preparation, made from infected larvae, is commercially produced in Finland and Great Britain.

Nuclease: A general term given to any enzyme that cleaves phosphodiester bonds in either DNA or RNA. Specifically, ribonucleases (RNases) cleave RNA and deoxyribonucleases (DNases) cleave DNA. Enzymes that remove nucleotides sequentially from the ends of oligonucleotides are called *exonucleases,* whereas enzymes that cleave bonds within an oligonucleotide chain are called *endonucleases. See also* Restriction endonucleases (which play a major role in genetic engineering methodology), S1 nuclease, Exonuclease III, Bal 31, Nick translation.

Nurse (feeder) callus: Callus masses used to stimulate plant cells to divide. If single plant cells from a suspension culture are plated at low density on semisolid agar, the cells do not divide. However, if callus masses (nurse calluses) are plated onto medium seeded with single cells, the single cells begin to divide in regions near the callus masses. This response shows a requirement for essential nutrients from the callus mass for cell division. *See also* Paper raft nurse technique.

Nutrient agar: A medium widely used for growth of nonexacting bacteria, which contains beef extract, peptones, sodium chloride, and agar. Some media manufacturers also include yeast extract in their formulations.

Nutrient film technique (NFT): A method for growing plants that ensures an adequate supply of both oxygen and water to the roots. Plant roots need both water and oxygen for satisfactory plant growth. Roots in soil are deprived of oxygen if there is abundant water. Conversely, good aeration is usually associated with lack of water. In NFT, plants develop their root systems in a very shallow stream of nutrient

solution. The solution depth is adjusted so that the lower part of the developing root mat grows wholly in solution. The upper part projects just above the surface, but remains covered by a liquid film. This exposed upper part allows for good aeration. The root mats produced by each plant are extensive and intertwined; this condition allows the plants to become self-supporting. *Compare with* Hydroponics.

Obligate: Used to qualify an environmental factor always required for growth (e.g., obligate aerobe means that oxygen is essential).

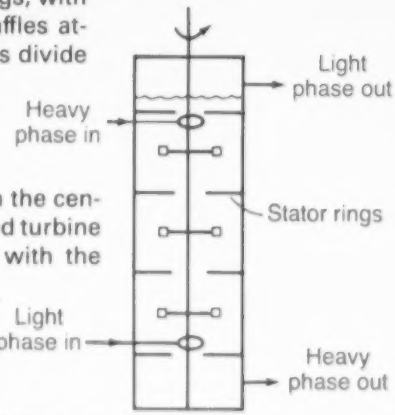
Obligate anaerobe: An organism, normally a bacterium, that grows and reproduces in the absence of oxygen. In the presence of even minute traces of oxygen, it may be inhibited or killed. *See also* Anaerobe, Facultative anaerobe.

Octopine: *See* Opines.

Off-gas: A term used to denote the gaseous product from a chemical or biological reaction.

Off-line analysis: The measurement of an analytical parameter of a process using a technique in which a discrete sample is taken and then removed to an analytical instrument for determination. A technique used for monitoring in which continuous measurement of the parameter is not required, or in which suitable on-line or in-line analytical techniques are not available. *Compare with* In-line analysis, On-line Analysis.

Oldshue–Rushton contactor: An agitated liquid–liquid contactor consisting of a vertical shell fitted with horizontal rings, with a central opening, and vertical baffles attached to the shell walls. The rings divide the column into a series of mixing zones, and the vertical baffles improve mixing by reducing the rotational movement of the fluids imparted by the agitators. In the center of each mixing zone a flat-bladed turbine is mounted on a common shaft with the other turbines and driven by an external motor. The inlet feed distributors are placed just above the top turbine for the heavy phase and just below the bottom turbine for the light phase. Calm settling zones are situated above the top and below the bottom stator rings.



Oleaginous (or oleagenous): A term used to describe organisms containing or producing oils.

Oligodeoxyribonucleotide synthesis: *See* Oligonucleotide synthesis.

Oligomer: A polymeric chain of a few monomeric repeat units. The chain length need not be defined.

Oligonucleotide-directed mutagenesis: *See* Site-directed mutagenesis.

Oligonucleotide probe: A short, radiolabeled, synthetic oligonucleotide that base-pairs with a region of a gene sequence and can therefore be used to detect, by hybridization, a clone containing the gene of interest (*see also* Colony hybridization) or an isolated gene or gene fragment (*see also* Southern blotting).

Oligonucleotide synthesis: The chemical synthesis of chains of oligodeoxyribonucleotides for use as DNA probes, synthetic genes, and in site-directed mutagenesis. More correctly, oligodeoxyribonucleotide synthesis. Because synthetic methods for oligodeoxyribonucleotides are more highly developed than those for oligoribonucleotides,

the term "oligonucleotide" has become synonymous with "oligodeoxyribonucleotide". The two main syntheses used are the phosphite triester method and the phosphotriester method. *See also* Phosphite triester method, Phosphotriester synthesis, Gene probe, Site-directed mutagenesis.

Oligosaccharide: A carbohydrate comprising a small number of monosaccharide units linked together. Longer chains and branched chains of monosaccharides are called polysaccharides.

On-line analysis: The continuous measurement of an analytical parameter, whereby a sample is taken continuously via a sample line to the analytical device to assist in process control. Not as satisfactory as in-line analysis. With the introduction of a sample line, care must be taken to ensure that a representative sample of the process is fed into the sample line and that no changes occur in the sample during its residence in the line. Finally, because of the presence of a sample line, the overall response time must be greater than with the in-line configuration. However, on-line analysis is still to be preferred in most cases to off-line analysis. Also the continuous transfer of data from a sensor to a recording device or computer. *Compare with* In-line analysis, Off-line analysis.

Open circular DNA: *See* Covalently closed circular DNA.

Operon: A group of functionally related genes regulated and transcribed as a unit.

Opines: Unusual amino acids, derived from arginine, synthesized in cells of crown gall tumors (*see Agrobacterium tumefaciens*). The ability to both induce and metabolize opines is encoded in the Ti plasmid of the bacterium *A. tumefaciens*. Infection of plant cells with *A. tumefaciens* therefore not only causes the cells to become malignant, but also induces the cells to use their own metabolism to synthesize opines. These substances are of no use to the plant, but can be metabolized and used as an energy source by the bacterium.

Optical activity: The ability of compounds possessing one or more asymmetric atoms (chiral centers) to interact with polarized radiation and cause rotation of the plane of polarization. The degree to which this plane is rotated is a function of the structure of the compound and its concentration in solution. *See also* Chirality, Dextrorotatory, Levorotatory.

Optical density: An obsolete term for the reduction in intensity of incident radiation on passing through an absorbent material. Now replaced by Absorbance.

Optical isomerism: A form of isomerism in which the isomers differ in their optical activity. *See also* Enantiomers, Chirality.

Optical rotation: The angle through which the plane of polarized radiation of a defined wavelength is rotated on passing through a solution that contains an optically active substance. *See also* Specific optical rotation.

Optoelectronic sensor: A sensor that uses optical principles coupled to an electronic transducer. For example, a sensor could consist of a detecting enzyme linked to a dye, which in turn is linked to a membrane. In the presence of a substrate, the enzyme generates a pH change that alters the color of the dye–membrane complex. This color change is recorded by using a transducer system that consists of a light-emitting diode (with wavelength equal to λ_{max} of the dye) and a photodiode.

Order of reaction: The rate of a reaction can be expressed as an empirical differential rate equation that contains a factor of the form $k[A]^a[B]^b$, where k is a proportionality constant, and a and b are constant exponents independent of concentration and time. These exponents are termed the order of reaction. Thus, in this expression, the order with respect to component A is a, of component B is b, and the total order of the reaction is $(a + b)$. The order may be integral, nonintegral, or zero. The order of reaction is determined experimentally and may differ from the actual number of molecules involved in the reaction.

Organ culture: In plant tissue culture, the unlimited growth of isolated organs (such as root tips, stem tips, and leaves) in a sterile nutrient medium. Organ cultures retain their characteristic structures and continue to grow in a manner comparable to that of their intact counterpart (*contrast with* Callus culture, Suspension culture). This growth allows the properties and functions of the individual organs to be studied in isolation. *See also* Tissue culture.

Organic pollution monitor: An instrument developed for water-quality monitoring applications and for the control of water- and wastewater-treatment processes. The monitor measures ultraviolet absorption at 254 nm, which correlates well with the total organic

carbon (TOC) for a range of samples from settled sewage and effluents to raw and treated river waters.

Organogenesis: The induction of root and shoot production in callus culture or explant tissue by the addition of appropriate ratios of auxins and kinins. Such induced cultures can, under appropriate conditions, develop to form plantlets and eventually fully grown plants.

Orifice plate: A device for measuring fluid flow rate, consisting of a plate that contains a precisely machined hole and is fixed perpendicularly across a pipe. As fluid passes through the pipe, a pressure differential related to the square of the fluid flow rate is set up across the orifice plate.

Origin of replication: A base sequence in DNA at which replication of DNA is initiated by DNA polymerase. In bacteria and viruses, usually only one replication occurs per genome. *See also* Replicon.

Osmosis: The process by which a fluid or solvent passes through a semipermeable membrane from a solution of low solute concentration to one of higher solute concentration. The movement tends to equalize the concentrations on either side of the membrane.

Osmotic pressure: The pressure required to prevent the osmotic movement of a fluid across a semipermeable membrane from a solution of low solute concentration to one of higher concentration. The osmotic pressure, a function of solute concentration, is dependent on the number of ions or molecules in solution.

$$\pi = \frac{cRT}{M}$$

where π is the osmotic pressure, c is the concentration of the solute, R is the gas constant, T is the temperature, and M is the molecular weight of the solute particles.

Osmotic shock disruption (cells): A technique that uses osmosis across the outer membrane of the cell in order to disrupt cells and release intracellular material. Transfer of water across the outer membrane builds up pressure within the cell and causes its eventual disruption. This technique requires less energy than some of the others available (e.g., Bead mills), but it tends to be less efficient and so is used mainly in the laboratory.

Osmotolerant: *See* Water activity.

Output rate: In a continuous-culture system, the quantity of cells produced in unit time.

Oxidation pond: An aerobic treatment method for farm-animal waste slurries. It involves a shallow static tank that relies on a large surface area to provide adequate aeration. The growth of algae on the surface is encouraged, as released oxygen improves the system. In emergencies, sodium nitrate may be added to provide additional oxygen by nitrate respiration of some bacteria.

Oxidation–reduction potential (redox potential): The electrode potential of a half-cell containing a mixture of the oxidized and reduced forms of the species concerned, measured relative to a standard hydrogen or calomel electrode. The potential, a function of the concentration of the species in solution, may be calculated for any particular conditions by the Nernst equation. *See also* Standard oxidation–reduction potential, Calomel electrode, Nernst equation.

Oxirane coupling: A coupling method used in the preparation of affinity columns. Bisoxiranes (bisepoxides) react readily with hydroxy- or amino-containing support matrices (e.g., Sepharose, Eupergit C) at high pH to yield derivatives with a long-chain hydrophilic, reactive oxirane, which in turn can be reacted with nucleophile ligands (amines, phenols, etc.).

Oxygen analyzer: An instrument incorporating devices capable of determining oxygen gas in a gas stream or in solution. Several techniques are available, for example:

: **Paramagnetic**: Oxygen is the only common gas that is paramagnetic; others are nitric oxide (NO) and nitrogen dioxide (NO_2). The oxygen analyzer is specific to oxygen determination in the absence of these other gases. The technique relies on the tendency for oxygen molecules to be attracted into a strong magnetic field. This attraction, although small in itself, can be used to affect other measurable parameters, such as the cooling of a heated wire (magnetic wind device), or cause the rotation of a balanced dumbbell. Calibration of these devices will allow conversion to oxygen concentration in the gas stream.

: **Electrolyte fuel cell–oxygen electrode**: *See* Dissolved oxygen electrode.

: **Process gas chromatography**: A gas mixture can be separated into its components by gas–liquid chromatography. By suitable choice of a detector the components, including oxygen, can be determined.

: **Process mass spectrometer**: Oxygen can be determined in a gas mixture by using a process mass spectrometer, which generally consists of a quadrupole instrument that gives a rapid response time with a relatively low resolution.

Oxygen transfer: The transfer of oxygen into solution in a fermentor, expressed in terms of the volumetric oxygen transfer coefficient K_La. This coefficient is a function of the intensity of agitation, rate of aeration, gas–liquid interfacial area, and rheological properties of the fermentation broth. A number of correlations have been proposed, depending on the size of the gas bubbles (small bubbles have <2.5-mm diameter and large bubbles have >2.5-mm diameter). In addition, in industrial fermentors, air bubbles usually form swarms or clusters. Here the correlation will vary from those of single bubbles, but they are still size-dependent with the same critical diameter of 2.5 mm. *See also* Surfactants.

Oxygen uptake rate (OUR): The rate of change in dissolved oxygen content of the medium within a fermentor as the process proceeds.

Oxygenic reactor: A reactor in which oxygen is used in place of air to produce the dissolved oxygen required for biological processes.

Packed cell volume (PCV): The percentage volume of cells in a given volume of culture after sedimentation (packing) by use of low-speed centrifugation.

Packed column: A column filled with a loose solid matrix of rings, saddles, etc., made of inert material. This packing, when used as a contacting device, provides a large surface area for adsorption, partitioning, or coalescence.

PAGE: Common abbreviation for polyacrylamide gel electrophoresis.

Panning technique: A method for purifying specific cell types by affinity chromatography. For example, anti-mouse-immunoglobulin antibodies adsorbed onto polystyrene dishes selectively bind cells that were previously treated with specific mouse monocloncal antibodies against a cell-type-specific surface antigen. Nonbound cells are washed away.

Papain: A thiol protease (MW 23,000) isolated from papaya latex. Its major uses are in the brewing industry (to stabilize and chillproof beer to prevent haze production) and in meat tenderization.

Paper raft nurse technique: A method for culturing single plant cells. Single cells are isolated from cell suspensions with a needle or fine

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capillary. Then each cell is placed on the upper surface of a square of filter paper that is resting on an actively growing callus (nurse callus). In this way the single cell receives growth factors produced by the callus, as well as growth factors from the nutrient medium. The cell divides to form small colonies, which can be subcultured onto fresh media to give callus isolates derived from single cells.

Paramagnetism: The interaction of an applied magnetic field with unpaired electrons in a substance. This interaction induces a magnetic field that reinforces the applied field so that the substance is attracted into the applied magnetic field. The strength of this interaction is proportional to the number of unpaired electrons and the temperature. This phenomenon is shown by organic free radicals, molecular oxygen, and transition metal ions and complexes (including metalloproteins). *See also* Diamagnetism, Ferromagnetism.

Parasexual hybridization: All nonmeiotic genetic recombination processes in vegetative cells. Few organisms currently used in biotechnological processes exhibit overt sexual recombination abilities, but most achieve limited recombination by parasexual mechanisms such as conjugation, transduction, transformation, mitotic recombination, and protoplast fusion.

Partially miscible substances: Fluids that, when mixed, form a single phase over a defined range of relative concentrations. Two phases occur outside the range of miscibility, and such systems may be used in the partitioning of a third component. *See also* Two-phase aqueous partitioning.

Partial pressure (gas): A measure of the amount of a certain gas in a mixture of gases. It is defined as the pressure that the gas would exert if it alone occupied the volume of the mixture of gases at the same temperature.

Partition chromatography: Any form of chromatography that relies on the partition of a single compound between two immiscible phases. This term should not be applied when different forms of the compound are distributed between the two phases.

Partition coefficient: The ratio of concentration of a substance in a single defined form between two immiscible or partially miscible phases. This term is not synonymous with distribution coefficient. *See also* Distribution coefficient.

Partition constant: Similar to partition coefficient, with concentrations replaced by activities. This term is not synonymous with distribution constant. *See also* Distribution constant.

Partitioning effect: The effect on the environment surrounding an enzyme when the enzyme is immobilized on a solid support. Depending on the nature of the support material, the partitioning effect may attract or repel substrate, product, ions, inhibitors, or other molecules to the support surface and thus concentrate or deplete them in the vicinity of the enzyme. For example, attraction of positive ions (and thus hydrogen ions) will reduce the pH in the immediate vicinity of the enzyme. The kinetics of the enzyme obtained under these conditions are referred to as *inherent* kinetics. *See also* Intrinsic kinetics.

Pectin: A complex acidic heteropolysaccharide that consists of α-1,4-D-polygalacturonide polymers. It is often complexed with two other polymers, a highly branched L-arabinan and a β-1,4-D-galactan. The carboxyl groups of the galacturonic acid units are partially esterified with methanol. Pectin, a structural component in various fruits and vegetables, becomes partially solubilized during processing of fruit juices. This change spoils the appearance and filterability of the fruit juices and reduces the yield of juice. To overcome the problem, pectinase is added to the juice during mashing. The enzyme degrades 1,4-α-D-galacturonic bonds and solubilizes the pectin, reduces the viscosity of the juice, and leads to a more stable and concentrated product. Pectinase preparations are usually a mixture of *endo-* and *exo*-polymethylgalacturonidases obtained from *Aspergillus* spp.

Pectinases: *See* Pectin.

PEG: *See* Polyethylene glycol.

Pekilo process: A process for the production of single-cell protein that uses carbohydrates such as sulfite liquor or wood hydrolysates. The process is based on the fermentation of the mold *Paecilomyces varioti*. *See also* Single-cell protein.

Penicillin acylase (penicillin amidase, E.C. 3.5.1.11): An enzyme that catalyzes the deacylation of the side chain of penicillin G and leaves the penicillin nucleus, 6-aminopenicillanic acid (6-APA). 6-APA is used as the starting point for the synthesis of several semisynthetic antibiotics, such as ampicillin and cloxacillin. The immobilized enzyme, obtained from *Escherichia coli*, is used commercially in plug flow column reactors.

Penicillin amidase: *See* Penicillin acylase.

Penicillinases (E.C. 3.5.2.6): Also known as β-lactamases. Enzymes that hydrolyze the β-lactam ring of the penicillin structure. Production of such enzymes by microorganisms is responsible for the resistance of the organisms to penicillins and cephalosporins. Hydrolysis of the amide bond in the ring produces penicilloic acid, which has no antimicrobial activity. β-Lactamases are used commercially to inactivate penicillin in milk and thus prevent consumer allergic reactions. Natural inhibitors of penicillinase, such as clavulanic acid, are used in drug formulations to overcome microbial resistance.

Penicillin enrichment technique: A method for the isolation of bacterial auxotrophs from a mutagen-treated culture. Under normal conditions an auxotroph is at a disadvantage compared with the parental (wild-type) cells. However, because penicillin kills only growing cells, when the survivors of a mutation treatment are cultured in a medium containing penicillin and lacking the growth medium of the desired mutant, only those cells unable to grow (i.e., the desired auxotrophs) survive.

Penicillin G (benzylpenicillin): The original penicillin molecule, produced commercially from *Penicillium chrysogenum*. It is the starting material for a more active range of semisynthetic penicillin molecules. *See also* Penicillin acylase.

Penicillium: A fungal genus belonging to the Deuteromycotina. Many widespread species may cause spoilage problems. A few species have been exploited for production of antibiotics (e.g., *P. chrysogenum*, penicillin; *P. griseofulvum*, griseofulvin; *P. utricae*, patulin), enzymes (e.g., *P. glaucum*, pectinase), and starter cultures (e.g., *P. camemberti*, *P. roquefortii*).

Percolating (trickling) filters: A widely used reactor design for the aerobic processing of urban and industrial wastes. The waste is passed through filter beds of clinker, stone, gravel, or plastic, where the biomass adheres to the surface of the filter material, covered only by a thin film of water. This absorbed solid is broken down by extracellular enzymes from endogenous microorganisms (mainly the Zoogloea) and metabolized. This process results in the release of excretory products. In this way the wastes are completely degraded to simple salts, gases, and water. Although this method is commonly used, a major problem can develop. Excessive growth of microorganisms in the filter restricts ventilation and flow. Such filters are

also used to remove waste gases from industrial processes. Water containing dissolved inorganic nutrients is passed down a column. It forms a thin film on the packing material, which is covered by a biofilm of microbial flora. Waste gas is forced to rise through the column, against the water flow. Water-soluble components and oxygen are transferred to the liquid phase and then to the biolayer, from which they are eliminated by aerobic reactions.

Perforated plate column: *See* Sieve plate column.

Periplasm: *See* Periplasmic space.

Periplasmic space: The space between the cytoplasmic and outer membrane in Gram-negative bacteria. The fluid in the periplasmic space, called *periplasm*, contains a number of secreted enzymes.

Peristaltic pump: A device for transferring fluid using a rotating drum with rollers attached to the circumference, rotating within a cylinder. A flexible tube is positioned between the drum and the containing cylinder so that rotation of the drum causes the rollers to squeeze the tube. The roller pressure carries forward discrete volumes of the fluid contained in the tube. These pumps have the advantage that the fluid has no contact with moving parts of the pump and is contained within a tube. The flow rate can generally be varied easily between limits set by the rotational speed of the drum. In addition, the system is easy to sterilize. However, the fluid flow will generally not be pulse-free, the amplitude of the pulses depends on the number of rollers, and the pump is not able to transfer fluid against a significant back pressure.

Permeate: The portion of a fluid that traverses a membrane. The opposite of retentate.

Permeation chromatography: *See* Gel filtration.

Permselective membrane: *See* Semipermeable membrane.

Peroxidase: An enzyme that breaks down hydrogen peroxide to oxygen and water. The presence of the enzyme is detected by coupling the release of oxygen to the oxidation of a hydrogen donor such as tetramethylbenzidine (TMB) or *o*-phenylenediamine (OPD), which results in a colored product. The horseradish enzyme is often used in enzyme-linked assays such as ELISA or the immunodetection of protein blots. It can also be used to hydroxylate aromatic compounds.

At 0 °C, para-substituted aromatics are hydroxylated at the meta position and vice versa.

Pervaporation: A process by which components of a mixture are separated by the use of a membrane between the feed and product streams. The product side operates at a reduced pressure to produce a vapor on this side. The membranes have an asymmetric structure, with a homogeneous skin supported on a microporous substructure. The driving force for the process is a partial pressure gradient of 10^{-3}–10^{5} Pa across the membrane. The separation processes involve both solubility and diffusivity of the components within the polymeric matrix. The process is used for the separation of organic products from aqueous solution, especially with azeotropic mixtures. *Compare with* Membrane distillation.

Phage: *See* Bacteriophage.

λ-Phage: A bacteriophage containing double-stranded DNA that infects *Escherichia coli*. Derivatives of λ-phage are used extensively as cloning vectors. The λ genome is 49 kbp long. *See also* λ Insertion vector, λ Replacement vector.

Phanerochaete chrysosporium: *See* Lignin.

Phase diagram: A diagram that represents the conditions of equilibrium between various parts of a system separated by definite boundary surfaces under defined experimental conditions. Of particular use with partially miscible systems to determine the relative concentrations under which the system will separate into two liquid phases.

Phase ratio: The ratio of one phase (solvent) to another (feed) in, for example, liquid–liquid extraction. Usually expressed in terms of volume ratio.

Phase-transfer catalysis: *See* Ion-pair partitioning.

pH electrode: *See* Combined electrode.

Phenol extraction: A commonly used method for deproteinizing a cell extract as a first step in the purification of DNA or RNA. Phenol, or a 1:1 mixture of phenol and chloroform, is mixed gently with the cell extract; then the layers are separated by centrifugation. Precipitated protein forms as a white mass at the interface between the aqueous and organic phases, with the DNA and RNA in the aqueous phase.

Phenotype: The physical characteristics or behavior of a cell or an organism.

Phillips and Johnson tube: A device used for the on-line monitoring of oxygen in a fermentor. It consists of a coil of polytetrafluoroethylene (PTFE) immersed in the culture medium, through which a stream of pure nitrogen is passed. Oxygen diffuses through the polymer wall into the nitrogen stream at a rate proportional to its partial pressure in solution. Analysis of the mixed gas stream can then be made outside the fermentor by appropriate methods.

Phosphatase: Any enzyme (esterase) that catalyzes the hydrolysis of monophosphate esters. *See also* Alkaline phosphatase.

Phosphite triester synthesis (phosphoramidite method): One of the two main methods (the other being phosphotriester synthesis) for synthesizing oligonucleotides. The method involves linking nucleoside-3'-*O*(*N,N*-dialkylamino)phosphoramidite monomers. These monomers are used because of their resistance to hydrolysis and air oxidation, which pose a problem with other nucleoside phosphites.

Phosphoramidite method: *See* Phosphite triester synthesis.

Phosphorescence: A process similar to fluorescence. Radiation is emitted from a molecule after stimulation by adsorption of radiation of a defined wavelength. Phosphorescence differs from fluorescence in that the radiation will continue to be emitted after the exciting radiation is removed from the molecule. *See also* Bioluminescence. *Compare with* Fluorescence.

Phosphotriester synthesis: One of the two main methods (the other being the phosphite triester method) for synthesizing oligonucleotides. The method involves chemically linking suitably protected nucleotides in which the internucleotide phosphodiester bond is protected by esterification with a third group.

Photoautotrophs: Autotrophs that use light as their energy source for synthesizing biological molecules from carbon dioxide (e.g., plants and algae).

Photolysis: The cleavage of water by the light reaction of photosynthesis. The production of an energy source (hydrogen) from abundantly available water, by photolysis, is currently a major area of research in biotechnology.

Photosynthesis: The metabolic process whereby plants and algae convert atmospheric carbon dioxide into organic molecules, with the concomitant evolution of oxygen, using sunlight as an energy source.

Photosynthetic conversion efficiency: The percentage of the total solar radiation falling on a given area in a given time that is converted into harvestable organic material. It follows that the harvestable biomass is a measure of photosynthetic efficiency. Mean annual figures are 0.5–1.5% in temperate areas and 0.5–2.5% for subtropical crops.

Pinocytosis: The process of engulfment of external solid and liquid matter by a cell.

Plant-growth substance: An organic substance, either produced within a plant or synthetically produced and introduced into a plant. At low concentrations it will promote, inhibit, or qualitatively modify growth, or affect patterns of differentiation. Such compounds include auxins, gibberellins, cytokinins, abscisic acid, and ethylene.

Plant hormone: *See* Plant-growth substance.

Plaque: An area of clearing or reduced growth in a bacterial lawn caused by the lysis of cells by infecting phage particles.

Plasma cell: A terminally differentiated B-lymphocyte that produces large amounts of secreted antibody. One of the many cell types that make up the white cell component of blood.

Plasmalemma: The membrane of a protoplast. It is the only barrier between the external environment and the interior of the cell.

Plasmids: Small (MW 1×10^6 to about 200×10^6) molecules of circular, double-stranded DNA that replicate independently of chromosomal DNA, found in certain bacteria. Plasmids can be isolated easily by lysing bacterial cells and separating plasmid DNA from chromosomal DNA by cesium chloride gradient centrifugation in the presence of ethidium bromide. In particular, plasmids have found considerable use as cloning vectors. However, those used currently are not naturally occurring forms, but forms that have been extensively modified in vitro to give properties useful for cloning. Plasmids are generally identified by a code of the form pAB123, where p stands for plasmid, AB are initials identifying the worker or laboratory responsible for isolating the plasmid, and the number is the laboratory's code for that particular plasmid (e.g. pBR322, pSC101, pMB1,

pUK230). *See also* Compatibility, Episomes, Relaxed replication, Resistance plasmids, Col plasmids, Virulence plasmids.

Plasticizer: Substances incorporated into polymers to alter their workability, flexibility, etc. They generally consist of high-molecular-weight compounds such as phthalates, polyglycols, and phosphate esters. They may be leached out of the polymeric material during use and hence contaminate fluids in contact with items such as peristaltic pump tubing and plastic containers.

Plate and frame filter: A system used for filtration and membrane processing that consists of a sandwich structure of alternating supports (plates) for the membrane or filter cloth and frames for the slurry or product. The assembly is relatively inexpensive and easy to dismantle for cleaning, but has high operating costs. It can be difficult to provide safe containment for the overall system. *Compare with* Centrifuge.

Plate column: An extraction or distillation column constructed with a packing made of individual plates or trays to aid coalescence and distribution. *See also* Bubble-cap plate, Sieve plate column.

Plate efficiency: A measure of the performance of an adsorption or distillation column. If perfect contacting occurred at a tray or plate in such a column, then the plate efficiency would be 100% and the two product streams would be at equilibrium. However, in practice the plate efficiency is less than 100%, so more contacting devices are required to achieve the desired separation or adsorption than theoretically calculated. The difference (expressed as a percentage) is termed the plate efficiency.

Plate (theoretical): A term used in partitioning (e.g., separation, adsorption, or distillation) to define the number of individual equilibria that would be equivalent to the performance of a column used for a particular process. Thus, a 10-plate extraction column would achieve the same separation performance as 10 successive individual contacts between the solute and solvent. *See also* Height equivalent to a theoretical plate.

Plasticity: One of the fundamental parameters of rheology. When a force is applied to a fluid, flow cannot occur until the applied shear stress exceeds the yield stress of the material. The larger the yield stress, the greater the plasticity.

Plastome: The genetic material (DNA) found in chloroplasts. Also referred to as ctDNA or cpDNA.

Pleiotropic: Refers to a single change or activity that influences more than one characteristic of a cellular phenotype.

Ploidy: The number of chromosomes in a cell. Similar to Karyotype: Euploid, the correct number; Aneuploid, an abnormally high or low number, with the individual chromosomes not in their normal proportions; Polyploid, a number increased by an integral factor.

Plug flow: A term used to describe the fluid flow regime when no axial mixing occurs and thus all the fluid elements have exactly the same residence time. *See also* Laminar flow, Turbulent flow.

Plug flow column (tubular) reactor: A biochemical reactor that comprises columns packed with immobilized biocatalyst particles. Substrate solution is passed into the column, where it is exposed to a high enzyme concentration, and product molecules are flushed out of the other end. Product concentration in the reactor is therefore kept to a minimum. This procedure reduces the chances of product inhibition, but substrate inhibition can be a problem.

Podbielniak extractor: A centrifugal countercurrent liquid extractor used for antibiotic recovery from fermentation broths. Flow rates in excess of 100,000 $dm^3\ h^{-1}$ are possible with the largest extractors.

Point mutation: An alteration in the DNA base sequence that results in a single base being replaced by another. As a result of this mutation, a single amino acid may be changed in the protein sequence that is coded for by the region of DNA containing the mutation.

POL: Name given to the region of RNA in a retrovirus that codes for RNA polymerase.

Polishing: The removal of the final traces of contaminant from a liquid to produce a very clean product, as in polishing filtration, polishing ion exchange, etc.

Pollen culture: A technique in which immature pollen is induced to divide and generate tissue, either on solid media or in liquid culture. Microspores are released from anther tissue and cultured on an appropriate medium, where they divide and generate tissue that can develop to produce a mature plant (*see* Anther culture). At present

the technique has only proved successful in a few species, and the closely related technique of anther culture is more generally used. These techniques allow the generation of haploid plants.

Poly(A) tail: A sequence of 200–300 polyadenylic acid residues added posttranscriptionally to the 3′-end of most eukaryotic mRNAs. *See also* Poly(U)sepharose.

Polyacrylamide gel: Gels formed by the polymerization of acrylamide monomers in the presence of a co-monomer *N,N′*-methylenebisacrylamide (bis), which acts as a cross-linking agent. Polymerization is induced by the addition of free radicals. Acrylamide gels are commonly used as a support in polyacrylamide gel electrophoresis of DNA and proteins. Polyacrylamide gels are used as a gel filtration medium, and ion-exchange derivatives of the gel are also available. By reaction with suitable compounds (e.g., production of the aminoethyl or hydrazide derivative) polyacrylamide gels can be converted to solid carriers suitable for binding ligands. *See also* Polyacrylamide gel electrophoresis.

Polyacrylamide gel electrophoresis (PAGE): Electrophoresis in acrylamide gels is used to analyze both protein and nucleic acid mixtures. As samples are electrophoresed through the gel, molecules separate according to size because of the sieving properties of the gel. The pore sizes in the gel, and hence the molecular weight range of molecules that can be separated in a given gel, are determined by the acrylamide and bis concentrations. Polyacrylamide gel electrophoresis is most frequently used during DNA sequence determination and in protein analysis by SDS gel electrophoresis.

Polyclonal antiserum: *See* Antiserum.

Polydentate ligand: A general term used to describe a molecule (ligand) capable of binding to a metal ion by more than one donor site. More precise terms such as bi-, tri-, tetra-, penta-, and hexadentate are used to indicate binding at two to six sites.

Polyelectrolyte: A macromolecule containing many ionizable groups that may be anionic or cationic, strong or weak acids, or bases. The term is normally used for soluble materials such as proteins or nucleic acids.

Polyethylene glycol (PEG): A polymer of ethylene glycol, sold as different molecular weight sizes of polymer (e.g., PEG 4000, PEG 6000).

Used in particular to fuse protoplasts and cells (e.g., in the formation of hybridomas), in two-phase aqueous systems, and to precipitate phage particles during their isolation.

Poly-β-hydroxybutyrate (PHB): A thermoplastic polymer of β-hydroxybutyrate esters, accumulated by a range of organisms as an energy reserve. It is prepared from *Alcaligenes eutrophus,* which can accumulate up to 70% of its dry weight as PHB. Cells are ruptured and PHB is extracted with a halogenated hydrocarbon. Because it is biodegradable, this polymer has a range of potential uses (e.g., as a medical suture).

Polylinkers: Synthetic double-stranded oligonucleotides that contain a number of different restriction sites. They are introduced into vectors to generate new and more versatile vectors with an increased number of potential restriction sites. The modified vectors can therefore be used to clone DNA fragments generated by a range of restriction enzymes.

Polymer: An assembly of a large number of repeat units (monomers) that may be represented visually as chains, sheets, or three-dimensional structures.

Polynucleotide kinase: An enzyme, prepared from *Escherichia coli* infected with T4 phage, that adds phosphate groups to free 5′ terminal hydroxyl groups in DNA molecules.

Polyploid: *See* Ploidy.

Polysaccharides: Polymers built from monosaccharide units (e.g., pentoses, hexoses, amino sugars). Polysaccharides produced by fermentation have a range of industrial applications. *See also* Xanthan gum, Dextran, Alginate, Zanflo, Polytran.

Polytran: Also known as Scleroglucan. A linear β-1,3-glucan (polysaccharide) with a D-glucopyranose group linked β-1,6 to every third or fourth residue. It is produced as an exopolysaccharide by the fungus *Sclerotium glucanicum* grown in submerged culture, and is used in oil recovery, ceramic glazes, seed coatings, and printing inks.

Poly(U)sepharose: An affinity matrix used to purify mammalian mRNA. It comprises poly(uridylic) acid covalently bound to agarose. Most mammalian mRNA molecules contain a "poly A tail" of 200–300 polyadenylic acid residues at their 3′ end. This tail region hydro-

gen bonds to the poly U by complementary base pairing and thus binds the mRNA to the column, whereas other molecules pass through the column unhindered.

Porous glass or silica: Support materials for chromatography, usually treated with a silanizing reagent to minimize adsorption by residual hydroxyl groups on the glass or silica. Also used as a medium for exclusion chromatography.

Potentiometric sensors: A type of sensor that gives, as an output, a potentiometric difference; for example, many types of electrodes, including ion-selective and glass.

Power input: A measure of the energy applied to a system, as in the stirrer or agitator of a fermentor. It is measured by a wattmeter attached to the stirrer motor, torsion dynometers, or strain gauges on the inside of the hollow stirrer shaft.

Power number: A dimensionless number that represents the inertial forces transmitted to a fluid by stirring:

$$N_P = \frac{P}{\rho N^3 D^5}$$

where P is impeller power input, ρ is density of the continuous phase, N is impeller speed, and D is impeller diameter.

Precoat filter: A layer of filter aid applied to a filter cloth before carrying out a filtration to minimize clogging (blinding) of the filter cloth and thus maintain a high rate of filtration. May also be applied to a type of drum or rotary filter fitted with a scraper discharge. *See also* Drum filter.

Precursor: A compound that is formed prior to, and can be converted into, the product of interest.

Preflashing (prefogging): The exposure of photographic film to a brief flash of low-intensity light just prior to its use in fluorography. This treatment sensitizes the film to low-intensity light emissions.

Primary cell culture: A freshly isolated culture of cells derived directly from a particular organ, tissue, or the blood of an organism. Free cells can be obtained by treatment of tissue pieces with the proteolytic enzyme trypsin (trypsinization) or perfusion of the tissue with the

proteolytic enzyme collagenase. Primary cell cultures are usually heterogeneous and have a low growth fraction, but they are representative of the cell types in the tissue from which they were derived. Subculturing of the primary culture gives rise to a secondary culture.

Primary metabolites: The metabolites formed during the log phase (tropophase) of microbial culture. *See also* Tropophase.

Primer: A short (≈10) oligonucleotide that base-pairs to a region of single-stranded template oligonucleotide. Primers are necessary to form the starting point for reverse transcriptase to copy adjacent sequences of mRNA, or for DNA polymerase to produce complementary-strand synthesis with single-stranded cDNA.

Probe: *See* Gene probe.

Procion dyes: Monochloro- or dichlorotriazine dyes that are extensively used in dye–ligand chromatography (e.g., procion blue, procion red, procion green).

Productivity: A measure of the production of biomass per unit time in a microbial culture. It is measured as grams of biomass per cubic decimeter per hour.

Prokaryotic cell: A cell whose genetic material is present throughout the cell and not organized into a discrete nucleus (e.g., all bacterial cells are prokaryotic). *Compare with* Eukaryotic cell.

Prolamins: One of the four major categories of seed storage proteins. *See* Seed storage proteins.

Promoter: A nucleotide sequence found upstream of a gene that acts as a signal for the binding of RNA polymerase. In *Escherichia coli*, promoter sequences are about 35 and 10 bp from the start of transcription and are about 7 bp long.

Prophage: Bacteriophage DNA integrated into the bacterial chromosome. *See also* Lysogenic infection.

Proteases: Enzymes that break down proteins by hydrolyzing specific peptide bonds. All proteases can be classified under one of four headings, based on specific groups present at the active site that are essential to the catalytic mechanism of the enzyme. They are:

: **(1) Serine proteases**: These enzymes all cleave peptide bonds by a common mechanism that involves a highly nucleophilic serine residue at the active site that is essential for enzyme activity [e.g., trypsin (E.C. 3.4.21.4), chymotrypsin (E.C. 3.4.21.1)].

: **(2) Metalloproteases**: These enzymes contain a metal enzyme, usually zinc, that is essential for enzymatic activity [e.g., carboxypeptidase A (E.C. 3.4.17.1), thermolysin (E.C. 3.4.24.4)].

: **(3) Acid proteases**: These proteases all contain a carboxyl group at the active site that is essential for activity [e.g., rennin (E.C. 3.4.23.4)].

: **(4) Thiol proteases**: Proteases that have a thiol(–SH) group at the active site that is essential for activity [e.g., papain (E.C. 3.4.22.2), bromelain (E.C. 3.4.22.4), and ficin (E.C. 3.4.22.3)].

Proteases have a wide range of industrial uses. One of the most widely used enzymes is Subtilisin Carlsberg (E.C. 3.4.21.14), a serine protease produced from *Bacillus licheniformis*. This enzyme is extensively used in enzyme washing powders. Other uses of proteases include wheat gluten degradation in the baking industry, chillproofing in the brewing industry, curd formation in the cheese industry, meat tenderization, removal of hair in the tanning industry, and the recovery of silver from spent photographic films.

Protein A: A protein produced by, and purified from, certain strains of *Staphylococcus aureus*. The protein binds to the F_c portion of certain classes of IgG molecule (*See* Immunoglobulin), without impairing the ability of the antibody to bind to an antigen. Protein A has found particular use in immunoassays and in purifying IgG subclasses by affinity chromatography. Protein A is bivalent (i.e., each molecule will bind two IgG molecules).

Protein blotting (western blotting): The transfer (by either diffusion or electrophoretic transfer) of separated proteins from a gel medium (e.g., polyacrylamide) to a nitrocellulose (or nylon) sheet, where the proteins bind. The proteins, once concentrated on the surface of the solid support, may be further investigated by the use of probes such as antibodies. Such analysis of the proteins is not possible in the gel medium. Because the method is analogous to Southern blotting for DNA, the term western blotting is sometimes used. *See also* Northern blotting.

Protein engineering: Originally a term used to describe any chemical modification of a protein that resulted in an altered structure or func-

tion for the protein. Now it is used more specifically to describe the predetermined replacement by site-directed mutagenesis of specific amino acids in a protein. This replacement results in the synthesis of a protein with enhanced characteristics, such as increased stability, increased catalytic activity, or altered substrate specificity. *See also* Site-directed mutagenesis.

Protein inclusion bodies (refractile bodies): Dense, insoluble protein bodies of the order of 1 μm in diameter, often formed when eukaryotic proteins are produced by the genetic modification of microorganisms. Following cell concentration (centrifugation) and disruption, inclusion bodies are separated from soluble cell protein and particulate cell debris by centrifugation. The solubilization of protein from the inclusion bodies, followed by refolding of the product to the native conformation, are critical to the recovery and purification of the required protein.

Protein targeting: The attachment, by genetic manipulation, of a leader sequence to the N-terminus of a protein so that, after translation by cytoplasmic ribosomes, the protein will pass through a "target" membrane. In this way, nuclear-coded proteins can be targeted to enter specific organelles.

Protoclonal variation: *See* Protoclone.

Protoclone: A clone of cells generated from a single plant protoplast. Protoclones that produce regenerated plants that show differences in phenotype when compared with the parent plant are said to have undergone protoclonal variation. This is effectively the same as somaclonal variation.

Protoplast fusion: Two protoplasts may be fused to give a single hybrid cell containing a single fused nucleus. This fused protoplast can then regenerate a cell wall and grow as a normal cell. The method has been used to fuse different strains of filamentous fungi, yeast, streptomycetes, and bacteria (and thus produce improved strains by recombination). The same method is used to fuse plant protoplasts (somatic fusion) that can regenerate and produce full plants. Fusion methods include the use of polyethylene glycol and electrofusion.

Protoplasts: Microbial or plant cells devoid of their cell walls. They are prepared by treating cells with cell-wall-degrading enzymes (e.g., snail gut enzyme, Novozyme) in isotonic solution.

Pruteen process: A process devised by Imperial Chemical Industries (ICI) that uses extremely-large-scale culture (1500 m^3) for the production of bacterial single-cell protein ("Pruteen") for use as animal feed. *Methylophilus methylotrophus* is the microorganism used, with methanol as a substrate.

Pseudoplastic fluid: A fluid in which viscosity decreases with increasing shear rate, such that shearing thins the fluid. The relationship between the applied shear (τ) and the shear velocity (γ) follows a power law of the form

$$\tau = k\gamma^n$$

where k is a proportionality constant. For example, when n is less than 1 (the Steiger dry model),

$$\gamma = a\tau^3 + c\tau$$

Pseudoplastic fluids generally show Newtonian behavior at high and low shear rates on either side of the power law region.

Pullulan: A neutral linear homopolysaccharide produced commercially by the growth of *Aureobasidium pullulans*. It is an exopolysaccharide. Pullulan consists of glucose units polymerized into repeating maltotriose units. Within each maltotriose unit, the glucopyranose units are linked by α-1,4 glucosidic bonds. The repeating maltotriose units are linked by α-1,6 glucosidic bonds. Pullulan forms strong resilient films and fibers that can be molded and, in particular, shows low oxygen permeability when cross-linked with other materials to form thin polymeric films. Cross-linking is an important feature for food-packaging materials. Also used in the preparation of adhesives, fibers, molded articles, coatings, and films.

Pullulanase: An enzyme that acts specifically on the α-1,6 bonds of the amylopectin of starch and therefore is called a "debranching" enzyme. It is prepared commercially from *Klebsiella pneumoniae* and is used in conjunction with glucoamylase (which only slowly hydrolyzes α-1,6 bonds) in the saccharification of starch.

Pulsed column: A contactor for liquid–liquid extraction. The column usually contains some form of coalescence and distribution devices such as plates and is fitted with an oscillating pump that provides a pulsing action on the continuous phase. This action causes the continuous phase to oscillate during its progress through the column.

The oscillation applies a mild form of agitation to the system and thus improves the efficiency of the process. *See also* Pulsed plate column.

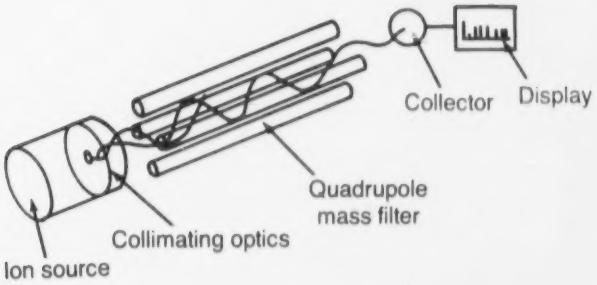
Pulsed plate column: An alternative design to the pulsed column. The stack of plates is capable of vertical oscillation and thereby promotes agitation in the column in the same way as the pulsed column. Both the pulsed column and the pulsed plate column may be designed with solid disks or modified as in the perforated plate or sieve plate designs.

Pulse-field gel electrophoresis: An electrophoretic technique for separating high-molecular-weight DNA fragments. The technique involves two electrical fields applied alternately at different angles for defined periods of time. These pulsed fields force large molecules to change direction repeatedly as they pass through the gel pores. Because DNA is a "long" molecule, these sudden changes of direction allow greater movement of small DNA molecules. They can change direction and travel more easily through the pore structure of the gel, whereas larger molecules move much more slowly. Small chromosomes, such as those found in yeast, can be separated with this method. Fine control of pulse times allows the creation of resolution "windows", which can be created anywhere between 5000 and 5 million bp. Normal agarose gel electrophoresis of DNA generally separates DNA fragments of less than about 20,000 bp.

Pure culture: A culture containing a single species of organism.

Pyrethrin: A commercially useful insecticide isolated from the plant *Chrysanthemum cinerariaefolium*.

Quadrupole mass spectrometer: A configuration of mass spectrometer commonly used for process instruments for the detection and analysis of process streams; for example, gases in the exhaust from fermentors. The operating basis of the instrument is as follows. Following ionization and fragmentation of the molecule, the ions are fed into the mass analyzer, which consists of four electrically conducting rods that form the corners of a square rectangular box. Opposite pairs of rods are connected to an electrical supply that carries both dc and radio frequency (rf) voltages, arranged so that at any instance one pair of electrodes is positive and the other negative. Ions are injected



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along the axis of the rod electrodes, where they meet the alternating electrical field. This field is arranged to filter out all ions except the one that resonates at the particular applied rf frequency. These ions pass down the axis of the rods and emerge at the end of the mass analyzer, to be detected and counted in the ion collector. Variation of the rf frequency allows the entire mass spectrum to be scanned at rates up to 1000 mass units per second, but with a lower resolution than that attainable with double-focusing instruments.

Quaternary ammonium salts: Ionic compounds with cations derived from the reactions of tertiary amines with, for example, alkyl halides to give compounds like $R_4N^+X^-$. These compounds have many uses (e.g., cationic surfactants, ion-partition reagents).

Quenching: In fluorescence, a process by which excited molecules lose their excess energy by collision with other species; the amount of fluorescent radiation emitted is thereby reduced. Oxygen is a particularly good quenching agent and therefore should be removed from solution before analysis. Also a term in scintillation counting; results in the observed counting rate being less than the true disintegration rate of the analyte. Here the emitted photons are intercepted in the solution by the presence of quenchers, dilution effects, etc., before reaching the photomultiplier.

Quinine: A plant alkaloid, isolated from the bark of the *Cinchona ledgeriana* tree; used as an antimalarial compound and as a bittering agent in the food and drink industry.

Racemate: An equimolar mixture of the dextro- and levorotatory optical forms of a compound that does not exhibit any overall optical activity.

Radioactive labeling: The incorporation of a radioactive isotope of an element into a chemical compound to follow the progress of the compound through a series of operations or reactions.

Radioimmunoassay (RIA): An assay method, much used in clinical and research laboratories, for using antibodies to detect small concentrations of substances (antigens). A known amount of radiolabeled antigen is added to the test solution, together with an antibody to the antigen. The radiolabeled and unlabeled (test) antigen compete for binding to the antibody molecules. The amount of radiolabel that binds to the antibody is determined; it is inversely proportional to the amount of test antigen. The greater the amount of test antigen present, the less radiolabeled compound will bind to the antibody, and vice versa.

Raffinate: The product stream that contains the lower concentration of the product when it leaves a process; normally applied to waste streams from extraction processes.

Read-through: A term describing a situation that sometimes occurs in transcription, in which the RNA polymerase molecule continues to transcribe beyond the expected termination point.

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Real time: In computing, the term means that computer calculations are keeping pace with actual events. For example, in computer graphics, the term is used to describe the ability to instantaneously and continuously rotate and translate a three-dimensional structure in response to an operator's commands. This effect is achieved by the rapid computation of new atomic coordinates. Such computation results in a rapid change in the graphics display that simulates motion of the molecule.

Reassociation: Describes the pairing of complementary single strands of DNA to form a double helix.

Recombinant: Transformed cell with recombinant DNA molecule.

Recombinant DNA: A DNA molecule formed in vitro by ligating DNA molecules that are not normally joined.

Recombinant protein: Any protein synthesized in a recombinant by expression of a cloned gene.

Recombination: Any process that helps to generate new combinations of genes that were originally present in different individuals.

Recycle bioreactor: *See* Loop reactor.

Redox-mediated sensors: Sensors utilizing a transducer device by which electrons generated by an oxido–reductase enzyme (or enzyme system) are transferred to an electrode surface by mediators such as cytochromes or ferrocene and its derivatives.

Redox potential: *See* Oxidation–reduction potential.

Reflux: A process by which part of a product stream from a reactor is fed back into the system to improve the performance of the process. For example, in fractional distillation, condensed liquid is returned to the top of a column. It comes into contact there with rising vapor of the components and thus aids separation of the components in the mixture. Also used in liquid–liquid extraction.

Rejection coefficient (membranes): A measure of the amount of a species in a feed solution to a semipermeable membrane that does not permeate the membrane.

$$R = 1 - \frac{C_p}{C_f}$$

where R is the rejection coefficient, C_p is the concentration of permeate, and C_f is the concentration of feed. In multicomponent systems, all species have their own individual rejection coefficients.

Relative viscosity: The ratio of dynamic viscosity of a solution to that of the solvent, each measured at the same temperature.

Relaxed plasmid: *See* Covalently closed circular DNA.

Relaxed replication: Plasmid replication is said to be relaxed when it is not stringently coupled to chromosomal DNA replication. Plasmids therefore exhibit relaxed replication by continuing to replicate once the bacterial cell stops dividing. This activity results in multiple copies (up to ≈3000 molecules) of a plasmid present in each cell.

Renewable resources: Biomass for biotechnological processes that can be produced on a regular basis as required (e.g., straw, sugar cane, microbial biomass). Compare with nonrenewable resources such as fossil fuels, natural gas, petroleum, etc.

Rennet: A crude commercial enzyme preparation from the fourth stomach (abomasum) of preruminant (suckling) calves, used extensively in the cheese industry for its milk-clotting activity. Its major proteolytic enzyme component is rennin (chymosin) (88–94%), but it also contains small amounts of pepsin. Because the availability of young calves for slaughter cannot match the commercial demand for rennet, rennet substitutes from microbial sources are increasingly used for the production of fermented milk products (e.g., a microbial product from *Mucor miehei*). However, such substitutes are not perfect because they differ slightly from rennet in their clotting activity. This variation modifies cheese yield and fat retention, and proteolysis products produced during ripening can have undesirable effects on flavor in the final product. *See also* Rennin.

Rennin: A proteolytic enzyme (E.C. 3.4.23.4) also known as chymosin; the main component of calf rennet. Rennin or rennet is much used in the production of fermented milk products because of its ability to coagulate (curdle) milk. Coagulation occurs principally as a result of the limited proteolysis by rennin of the κ-casein component of milk; it produces insoluble para-κ-casein and soluble macropeptides. Other casein fractions then precipitate as a result of exposure to calcium ions released by κ-casein hydrolysis. However, the overall process is probably more complex than this simple two-step process. The use of genetic engineering to produce rennin from microbial sources has been reported. *See also* Rennet.

λ Replacement vector: Modified λ DNA that has two recognition sites for the same restriction enzyme on either side of the nonessential (or "stuffer") part of the λ DNA molecule (*see* λ Insertion vector). The DNA fragment to be cloned (maximum length 21 kbp) is produced by cleavage with the same enzyme and replaces the excised "stuffer" region.

Replica plating: A technique for producing identical patterns of bacterial colonies on a series of Petri dishes. The surface of a Petri dish that contains colonies is pressed with a cylindrical block covered with sterile velvet, which causes about 10% of the bacteria in each colony to be transferred to the fabric. The velvet disk is then pressed against the surface of a bacteria-free plate. Some of each bacterial colony are thus transferred to the new plate; a replica pattern of bacterial growth is produced on this new plate. About six replicas can be printed from a single pad in this way.

Replicon: Any DNA molecule that has an origin of replication and is therefore capable of being replicated by DNA polymerase. If exogenous DNA is added to a bacterial cell, this DNA will not be replicated when the cell divides. Such exogenous DNA has no origin of replication, and therefore only the parent cell and none of the daughter cells will contain this DNA. In order for DNA to be replicated and passed on to all daughter cells, it must first be attached to a suitable replicon. Such replicons are known as vectors or cloning vehicles (e.g., plasmids or bacteriophage DNA).

Repressor: A protein that binds to DNA at a specific site (operator) to "switch off" a promoter and thus prevent transcription of the gene under the control of that promoter.

Reserpine: An antihypertensive agent prepared from the plant *Rauwolfia serpentina*.

Resistance plasmids (R plasmids): Plasmids that carry antibiotic resistance genes. Such plasmids confer antibiotic resistance to the host bacterium (e.g., plasmid pBR322 carries genes for tetracycline and ampicillin resistance). Such markers can be used in detection of transformants.

Resolution: The ability of a process to separate (resolve) two components with very similar properties. Used in analytical processes as a measure of selectivity. For example, the resolving power of a spectrophotometer is the ability to separate two spectral lines, and the

resolution of a chromatogram is the ability to separate two similar compounds.

Respiration: The oxidation of an organic or inorganic reductant by organisms to produce energy for metabolic reactions by a process involving an electron-transport chain.

Respiratory quotient: The ratio between the carbon dioxide production rate and the oxygen uptake rate in a fermentor, or in a Warburg or Gilson flask.

Restriction analysis: Determination of the sizes of DNA fragments produced by the cleavage of a given DNA molecule (e.g., a plasmid) by a given restriction endonuclease.

Restriction endonucleases: Also referred to as restriction nucleases or restriction enzymes. A number of enzymes, derived from a wide range of prokaryotes, that all cleave double-stranded DNA molecules. Different types of restriction endonucleases occur (types I to IV), but type II is of particular importance to genetic engineering. To date nearly 200 different type II enzymes have been isolated. The enzymes differ in the nucleotide sequence that they recognize and cleave. The sites recognized by most of the enzymes used in genetic engineering are palindromes (i.e., the 5′ to 3′ sequence in one strand of the DNA duplex is the same as in the complementary strand) of four, five, or six bases. Some enzymes cleave to give "blunt" or "flush" ends (e.g., *Hpa*I) or "sticky" (cohesive) ends, where a few unpaired nucleotides project from either end (e.g., *Eco*RI).

Arrows indicate the sites of cleavage. The generation of "sticky" ends is of particular use in cloning DNA. If a plasmid and the gene to be inserted are both cleaved with the same restriction enzyme, both DNA molecules will generate the same sticky ends, which will anneal by complementary base pairing. They can then be joined by DNA ligase to give a circular recombinant molecule that can be used to transform a bacterium.

Because so many restriction enzymes are available from a range of organisms, a standard terminology has been adopted. The genus and

species name of the organism is identified with the first letter of the genus and the first two letters of the species. This system generates a three-letter abbreviation in italics (e.g., *E. coli* = *Eco*). Strain or type identification is given in nonitalicized symbols (e.g., *Eco*R), and the number (sequence specificity) of the endonuclease is given in Roman numerals (e.g., *Eco*RI). The ability of restriction enzymes to cleave DNA specifically and reproducibly into discrete DNA fragments (a particular hexanucleotide sequence should occur on average only every $4^6 = 4096$ base pairs) has been an essential part of the development of genetic engineering.

Restriction enzymes: *See* Restriction endonucleases.

Restriction map: A map that shows the positions of different restriction sites (i.e., nucleotide sequences that are cleaved by various restriction enzymes) in a given DNA molecule (e.g., a plasmid). *See also* Restriction analysis.

Restriction nucleases: *See* Restriction endonucleases.

Retentate: The portion of material retained by a membrane. Opposite of permeate.

Retention time: A term used in column chromatography to denote the time taken for a particular component to emerge from the column; the time of injection is considered zero. This time depends on the experimental conditions used for the chromatogram but can, with standard conditions or internal standard compounds, be used to identify components in a mixture.

Retention volume: An alternative to retention time for the characterization of species emerging from a chromatographic column. In this case the volume of eluent required to elute a particular component is recorded. *See also* Breakthrough profile.

Reverse osmosis (hyperfiltration): A membrane process for the separation of a solute from solution. The process operates by the application of an external pressure greater than the osmotic pressure, which forces the solvent to pass through the membrane against its normal osmotic flow. Thus solvent molecules are removed from the concentrated solution. The process operates at high pressure, 1500–8000 kPa, and uses an asymmetric membrane with pore sizes less than 25 μm. Uses include the concentration of dilute solutions of salts, sugars, and amino acids; purification and recovery of water; and desalination.

Reverse-phase chromatography (RPC): A chromatographic method in which the support matrix (e.g., silica) is modified so as to replace hydrophilic groupings with large hydrophobic alkyl carbon chains. This modification allows the separation of proteins according to their hydrophobicity. The more hydrophobic proteins bind most strongly to the support and are therefore eluted later than the less hydrophobic proteins. The supports most commonly used for RPC of proteins or peptides have alkyl groups with chain length of either 8 (C_8) or 18 (C_{18}) carbon molecules. This method is commonly carried out by HPLC.

Reverse transcriptase: An enzyme prepared from Avian myeloblastosis virus, which synthesizes single-strand DNA from an RNA template. The normal process of transcription in a cell is the synthesis of RNA from a DNA template, hence the term *reverse* transcriptase. Such enzymes are unique to RNA viruses (retroviruses) that need to produce a DNA copy of their genetic materials (RNA) upon infection of a cell. The DNA copy thus directs the in-cell synthesis of protein and RNA necessary for the synthesis of new viral particles. The isolated enzyme is used extensively in genetic engineering methodology to synthesize (in vitro) complementary DNA (cDNA) from messenger RNA.

Reynolds number (Re): A dimensionless number used in fluid dynamics to determine the flow regime. It is a relation between the fluid properties of the system and the flow velocity:

$$\mathrm{Re} = \frac{LV\rho}{\mu}$$

where L is the linear dimension of the fluid channel, V is linear velocity, ρ is density of fluid, and μ is fluid viscosity. The Reynolds number defines the transition between laminar and turbulent flow as velocity increases. For laminar flow, generally $\mathrm{Re} < 2300$, and for turbulent flow $\mathrm{Re} > 10^4$. In agitated fermentors Re can be based on the root mean square fluid velocity, V_{rms}, and the average diameter of gas bubbles, $\overline{D}$:

$$\mathrm{Re} = \frac{\overline{D}\, V_{rms}}{\mu}$$

The Reynolds number in the vicinity of an impeller can also be considered by an impeller Reynolds number, Re_i:

$$\mathrm{Re}_i = \frac{\rho N D_i^2}{\mu}$$

where N is the rotational speed of the impeller in rpm and D_i is the impeller diameter.

R_f: A term used in chromatography to characterize components in a mixture when separated by paper or thin-layer techniques. It is defined as the ratio of the distance traveled by the component to that traveled by the solvent front.

Rheodestructive fluid: A fluid that undergoes irreversible breakdown when subjected to an applied shear stress. The fluid exhibits a decrease of viscosity with time that, when the stress is removed, does not return to its original value and may indeed continue to decrease slightly.

Rheogram: A plot of rheological parameters, for example, shear stress vs. shear rate.

Rheology: The science of deformation and flow of matter that gives rise to the three fundamental parameters of elasticity, plasticity, and viscosity.

Rheopectic liquid: A fluid that, when subjected to a constant shear rate, will rapidly exhibit an increase in apparent viscosity.

Rhizobium: A genus of bacteria involved in the process of nitrogen fixation in leguminous plants. Rhizobia are introduced deliberately into the soil of leguminous plants to encourage root-nodule formation. *See also* Nitrogen fixation.

RIA: *See* Radioimmunoassay.

Riboflavin: A vitamin (vitamin B_2) produced industrially in submerged culture from *Eremothecium ashbyii* (grown on carbohydrate-free media with lipid as an energy source), *Ashbya gossypii* (grown on glucose, sucrose, or maltose), *Candida* sp. (grown on sugar solutions), or *Clostridium acetobutylicum* (grown on grain mash or low-iron-containing whey). In the purified form it is used for human nutrition and therapy, and in the crude concentrated form it is used as an animal feed supplement.

Ribonuclease (RNase): *See* Nuclease.

Rising-film evaporator: A device for concentration of solutions, similar in operation to a falling-film evaporator in that the fluid forms a

thin film on the surface of the heat-exchanger tubes. However, in this case the overall flow of the liquid is upward, with the energy supplied by the system operating under vacuum. Circulation of the concentrated fluid is via a gravity return to the feed vessel. Also called climbing-film evaporator.

Roller bottles: A design that provides increased surface area for the growth of anchorage-dependent mammalian cells. The simplest design involves a continuously rolled cylindrical vessel that contains the cells and growth medium. This design makes nearly all the internal surface available for cell growth, even though only ≈20% is covered by medium at any one time. Other methods exist to increase the surface area further within a roller bottle. These include the incorporation of a spirally wound plastic film and packing of the bottle with a cluster of small parallel glass tubes separated by silicone spacer rings.

Root nodules: *See* Nitrogen fixation, *Rhizobium, Leguminosae.*

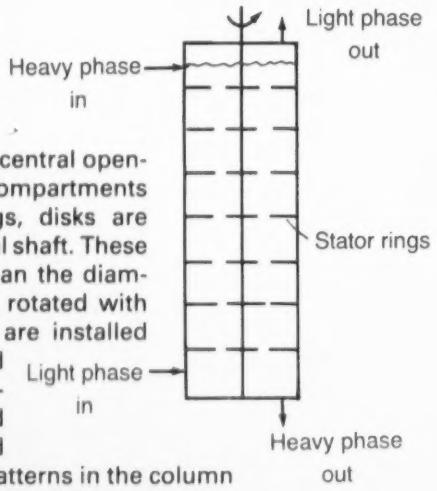
Rosette technique: A method for separating cells by affinity chromatography. For example, anti-mouse-IgG is fixed on ox red blood cells using chromic chloride. The cell population to be fractionated is treated with specific mouse monoclonal antibodies against surface antigens of the cells to be purified and added to the red blood cells. This procedure causes the formation of rosettes. Recovery of bound cells is achieved by selective lysis of the blood cells with ammonium chloride.

Rotary-disk biological contactor: A contactor used in the treatment of wastewaters and effluents that consists of a series of plastic disks 3–4 m in diameter, immersed up to 40% of the disk surface in a tank. On rotation at 2–5 rpm, the disks pick up liquid from the tank and bring it into contact with the air as a thin film. Microbes on the disk surface oxidize any organic compounds present in the liquid film. As microbial growth increases, the shearing effect of the liquid in the tank tends to remove the excess growth from the disks, which then can be removed from the waste stream by conventional settling tanks. The contactor is very popular for industrial wastes because of its small size and low energy requirements. However, problems exist with highly contaminated wastes because of excessive growth and insufficient oxygen to meet demand. Typical loading rates for this design are 13 g of BOD/m^2/day for domestic waste and partial treatment of 400 g of BOD/m^2/day for industrial waste.

Rotary filter: *See* Drum filter.

Rotating biological contactor: *See* Rotary-disk biological contactor.

Rotating disk contactor (RDC): This agitated contactor is used for liquid–liquid extraction. It consists of a vertical shell fitted with a series of horizontal flat plates with a central opening. In the middle of the compartments formed by these stator rings, disks are mounted on a common vertical shaft. These disks, with a diameter less than the diameter of the ring opening, are rotated with the shaft by a motor. Grids are installed above the top stator ring and below the lowest ring to provide calm settling zones, and the feed inlets are mounted tangentially so that the flow patterns in the column are not disturbed. Other designs of RDC are available (asymmetric RDC) in which the ring opening and disks are offset from the center.



Rubber: *See* Latex.

Runaway plasmids: A plasmid that has lost its ability to control its copy number at increased growth temperatures. The plasmids are present in the cell at low copy numbers (10–25) at the permitted temperature (30 °C), but increasing the temperature to 40 °C causes an increase of the copy number to as much as several thousand by uncontrolled plasmid replication. Such plasmids are necessary for the high expressions of cloned genes that code for products lethal to the cell at high concentrations. Cells are grown normally at the permitted temperature, then shifted to the nonpermitted higher temperature. Protein synthesis continues at the higher temperature for several hours after the increase in copy number, allowing overproduction of the cloned gene. This runaway replication is ultimately lethal to the cell.

S1 nuclease: An endonuclease, usually isolated from the fungus *Aspergillus oryzae*, that cleaves only single-stranded DNA. It is used to cut the hairpin formed during the synthesis of double-stranded DNA from cDNA, and in conjunction with exonuclease III to create deletions in cloned DNA molecules.

Saccharification: The hydrolysis of a polysaccharide to give a sugar solution. For example, the process whereby dextrin derived from starch is broken down to dextrose (glucose). *See also* Starch.

Saccharomyces cerevisiae: *See* Bakers' yeast.

Salting out: A process by which the aqueous solubility of a compound, usually organic (e.g., proteins), can be reduced by increasing the concentration of neutral salts.

Sand filter: A type of trickle filter or depth filter in which sand is used as the filtering medium.

Saprophytic: The capacity of any organism to live on dead or decaying organic matter.

Scale-up (factor): A term used to describe the translation of a process to a larger scale. It involves the variation of parameters required to

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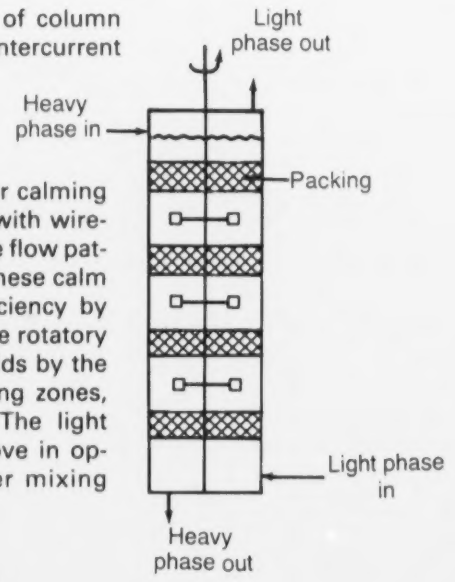
ensure optimum performance at the increased scale. It is generally accepted that the design of a commercial-scale reactor cannot be accomplished solely by a theoretical approach and that at least some laboratory data are required on the reaction involved in the process. Thus, although the behavior of a population of microorganisms should be invariant to scale, the behavior of factors affecting the surrounding environment is less easy to predict (e.g., oxygen transfer, shear behavior). Thus one approach to scale-up uses an extensive series of systematic scale-up and scale-down experiments to ascertain the effect of process variables on the product yield. This approach has the inevitable consequence of considerable costs in both time and equipment. An alternative approach uses a combination of modeling techniques based on an understanding of the kinetic behavior of the processes involved with practical experience gained from knowledge of the observed behavior of the process under actual process conditions.

Schmidt number (Sc): A dimensionless group that is a measure of the fluid properties of a system and relates the viscosity, μ; the density, ρ, of the fluid; and the diffusivity of solute A in solvent B, D_{AB}:

$$Sc = \frac{\mu}{\rho D_{AB}}$$

Scheibel contactor: A type of column contactor in which the countercurrent liquid phases are contacted in mixing zones agitated by rotating turbines on a common central shaft. The mixed phases then enter calming zones, which may be filled with wire-mesh packing to separate the flow patterns of the mixing zones. These calm zones minimize loss of efficiency by backmixing and eliminate the rotatory motion imparted to the liquids by the impeller. Once in the calming zones, the two phases separate. The light phase and heavy phase move in opposite directions into other mixing zones.



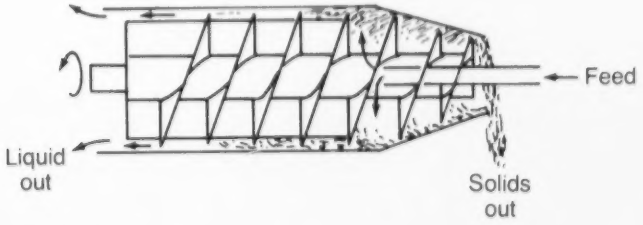
Scleroglucan: *See* Polytran.

Scopolamine: A plant alkaloid, isolated from *Datura stramonium* and used as an antihypertensive agent.

SCP: *See* Single-cell protein.

Screening: Any selective procedure used to identify specific organisms or metabolites in large populations.

Scroll screen centrifuge: A centrifuge consisting of a conical basket, either horizontal or vertical, which is fitted with a scroll. The scroll can be contoured either to advance the solids through the basket or to transport the solids down the basket. The feed slurry is fed at the apex of the cone, and the solids are discharged at the base. The liquid passes through perforations in the basket, and a relatively high throughput is achieved by the short residence time. However, the effectiveness of washing is low because of this short retention time for the solids, and also because of poor distribution of the wash liquors down the cone. The centrifuge has been adapted for liquid–liquid–solid separations, as in whole-broth extraction.



Scrubbing: The process of removing impurities from an extract phase by contacting with another solution phase such that the impurities are preferentially re-extracted from the solvent phase. *See also* Bioscrubbing.

SDS: *See* Sodium dodecyl sulfate.

Secondary cell cultures: A cell culture obtained by the repeated in vitro passage of primary cells. Most secondary cell cultures survive only for a limited number of cell divisions before dying. However, some will continue to grow (i.e., they transform) and establish a continuous *cell line* that is capable of being passaged indefinitely in vitro.

Secondary fermentations: Fermentations, other than the major fermentation, that occur during the production of fermented milk products. In the production of fermented milk products (e.g., cheese, buttermilk, sour cream, yogurt), the major fermentation is the bacterial breakdown of lactose to lactic acid, usually by streptococci and lactobacilli. Other reactions that may occur, either during the main fermentation or postfermentation, produce the distinctive flavors of individual products. These reactions are referred to as secondary fermentations; for example, propionic acid fermentation in milk leads to the typical flavor and eye formation (as the result of carbon dioxide production) in Swiss cheese.

Secondary metabolites: The metabolites produced during the idiophase (stationary phase) of microbial culture.

Sedimentation: The process of settling of particulate matter. Four types of settling may be recognized:

: **1. Discrete particle**: In systems with a low solids content, individual particles settle without any significant interaction with each other.

: **2. Flocculant settling**: A dilute suspension of particles that flocculate and coalesce so that their mass is increased, and thus the settling rate is increased.

: **3. Hindered settling**: Suspensions with particle concentration such that interparticle forces are sufficient to hinder the settling of neighboring particles, and the total mass settles as a single unit with a solid–liquid interface at the top. This is the typical behavior of a fermentation broth.

: **4. Compression settling**: The particles are present at such a concentration that a structure is formed, and further settling occurs only by compression caused by the weight of particles on top.

Sedimentation potential: The potential that is formed as the dispersed phase moves through the dispersion medium when the suspended particles are allowed to settle under the influence of gravity.

Seed storage proteins: The proteins of seeds that are used during germination to provide nitrogen for the developing seedling. They are classified into four major categories, based on their solubility properties: albumin, globulins, prolamins, and glutelins. Seed crops such as cereals and grain legumes play an important role in human

and animal nutrition. However, most contain limited amounts of amino acids that are nutritionally essential to humans. Most cereals are deficient in lysine, legumes are deficient in sulfur-containing amino acids, and rice has an overall low protein content. The improvement of the nutritional quality of seed storage proteins is therefore one of the aims of plant molecular biology.

Selectable marker: Any gene carried by a vector that confers a recognizable characteristic on a cell containing the vector (e.g., antibiotic resistance genes on plasmids).

Selection: Any means of identifying a clone that contains a desired recombinant DNA molecule. *See also* Selectable marker.

Self-transmissible plasmids: Plasmids that contain transfer (*tra*) genes that allow the production of pili involved in conjugal transfer of plasmid DNA. Laboratory-used plasmids have their *tra* genes deleted to prevent the possibility of self-transmission of recombinant plasmids if they should escape from the laboratory environment. *See also* Mobilization genes.

Semipermeable membrane: A membrane that is permeable to some substances but not others. The selectivity can be achieved by pore size or by the presence of charged species in the membrane. Also called permselective.

Sense strand: The strand of duplex DNA that is transcribed into mRNA.

Separation factor: The degree of separation achieved by a particular process or system, defined as the ratio of the concentration of the components (C_a/C_b) in the product phase (x) to those in the feed phase (y).

$$\text{separation factor} = \frac{(C_a/C_b)_x}{(C_a/C_b)_y}$$

Sephacryl: Cross-linked dextran polymer beads used as a gel-filtration medium. (Pharmacia trade name) *See also* Dextran.

Sephadex: Cross-linked dextran polymer beads used as a gel-filtration medium. (Pharmacia trade name) *See also* Gel filtration, Dextran.

Sepharose: Cross-linked agarose beads used as a gel-filtration medium. (Pharmacia trade name)

Sequencing gel: A long (up to 1 m), thin (0.2–0.5 mm) polyacrylamide slab gel; has the resolving power to separate single-stranded DNA fragments that differ by one nucleotide. The gel is kept hot, and urea is included in it, to prevent base-pairing. Such gels are used to separate radiolabeled DNA fragments in DNA sequencing methodologies. *See also* Maxam–Gilbert method, Dideoxy sequencing method.

Sequestering agent: Compounds that are able to form complexes with metal ions in solution and thus prevent their activity as simple cationic species. EDTA, for example, is effective for many metallic ions and can be used (1) as a means of ensuring that the metal ions may be held in a form appropriate for chemical reaction, (2) to prevent the deleterious catalytic effects of traces of the metal ion, (3) in the analysis for metal ions, and (4) in the preparation of culture media.

Serine proteases: One of the four possible classifications of proteases. Serine proteases all cleave peptide bonds by a common mechanism, which involves a highly nucleophilic serine residue at the active site. The serine protease most commonly used in industry is the microbial enzyme subtilisin Carlsberg, which is used extensively in enzyme washing powders. Other serine proteases include trypsin, chymotrypsin, elastase, and thrombin.

Serum-free media: *See* Fetal calf serum.

Sex pilus: A fimbrialike structure (tube) that is formed by one of the two mating types during bacterial conjugation, through which the genetic material is transferred.

Sexual hybridization: The bringing together of haploid nuclei from opposite mating types in one cell. The nuclei ultimately fuse to form the diploid nucleus, which will then undergo meiosis. During meiotic division, a rearrangement and reorganization of the chromosomes results in recombination of the genetic element.

Shear: The movement of a layer of fluid relative to parallel adjacent layers in the fluid.

Shear rate: The rate of change of shear (i.e., velocity gradient) in a fluid.

Shear stress: The force per unit area that causes the movement of a fluid by the process of shearing.

Sherwood number: The dimensionless Sherwood number (Sh) is associated with convective mass transfer and relates the mass-transfer coefficient (k_c) with the characteristic length of the system (L) and the diffusivity of the solute, A, in the solvent, B:

$$\mathrm{Sh} = \frac{k_c L}{D_{AB}}$$

Shikonin: A bright red naphthoquinone compound, used as a dye. Traditionally used in Japan as a medicine because of its antibacterial and anti-inflammatory properties. Although originally extracted from the root of the plant *Lithospermum erythrorhizon*, it is now produced commercially by plant-cell culture.

Shine–Dalgarno sequence: A base-sequence of about six to eight nucleotides located on mRNA, lying about four to eight nucleotides upstream from the initiation codon (AUG). The sequence acts as a ribosome-binding site at the first step of translation, by base-pairing with a complementary base sequence on the 16S rRNA chain.

Shotgun cloning: A cloning strategy in which genomic DNA is cleaved into fragments with a restriction endonuclease, and these fragments are inserted into a vector. The vector is then used to transform bacteria. The product is a large number of clones (library) that between them contain all, or most, of the genes present in the original genome.

Shuttle vector: Any vector that can replicate in more than one organism. For example, plasmid pJDB219 is made up of part of the 2-μm circle of yeast and the entire bacterial plasmid pBR322, and can replicate and be selected for in both yeast and *Escherichia coli*.

Sieve plate column: A column contactor containing a stack of perforated plates to aid distribution and coalescence, usually operated with pulsing of the plates or the continuous phase to increase residence time and agitation. Also referred to as a perforated plate column. *See also* Pulsed column, Pulsed plate column.

Signal sequence: A sequence of about 15–30 amino acids, mainly hydrophobic, found at the N-terminus of proteins that are exported from cells. As this N-terminal sequence is synthesized at the ribosome, it attaches to the endoplasmic reticulum (to give "rough" ER). The synthesized protein is synthesized directly into the interstices of the ER. The signal sequence is removed by specific proteolytic cleav-

age, once it has passed through the membrane, and therefore does not appear in the final secreted protein. Similar signal sequences are thought to exist to direct proteins across membranes between cell compartments. *See also* Protein targeting.

Silanization: The conversion of –OH groups, which could act as adsorption sites, commonly on silica or glass stationary chromatographic phases, to give the inactive $-O-SiR_3$ grouping by reaction with, for example, alkylsilicon halides R_3SiCl.

Silica gel: An amorphous form of hydrated silica formed by precipitation or chemical hydrolysis. When dehydrated, it forms hard granules that are chemically and physically inert, but are highly hygroscopic. This property leads to their main use in drying of solvents, gases, etc. The presence of –OH groups provides the active sites for adsorption, and thus allows the use of silica gel as a stationary phase for chromatography.

Silicone: Polymeric organosilicon derivatives containing –Si–O–Si– links. Depending on the nature of the polymeric chain, the products can be oils, greases, resins, rubbers, etc. They are chemically inert and immiscible with water, and as oils they have high flash points. One of their uses is as an antifoaming agent.

Silyl compounds: Compounds containing the $-SiH_3$ or $-SiR_3$ groups.

Simian virus 40 (SV40): A mammalian DNA virus used as the basis for a number of cloning vectors. It has potential use in transforming animal cells, in which it follows either a lytic or lysogenic cycle, depending on the species from which the cell is derived.

Single-cell protein (SCP): The microbial biomass component of a fermentation process that is produced commercially for human food or animal feed. After harvest the biomass is processed to a suitable food product. The name indicates its microbial origin, thus distinguishing it from proteins originating from higher multicellular plants and animals. Sources of SCP include "Toprina", an animal feed product produced by British Petroleum by the growth of yeast on *n*-alkane; "Pruteen", an animal feed product produced by I.C.I. by the growth of *Methylophilus methylotrophus* on methanol; "Pekilo protein", an animal feed product produced in Finland by the growth of the fungus *Paecilomyces varioti* on stripped sulfite waste liquor; and "Mycoprotein", a human food product produced by Rank–Hovis–MacDougall by the growth of the fungus *Fusarium graminearum* on glucose syrup.

The nucleic acid content of SCP should not exceed 3% of the dry weight; any greater nucleic acid content would lead to gout and gouty arthritis due to abnormal levels of uric acid in the blood caused by nucleic acid catabolism.

Site-directed mutagenesis: A technique for producing a single mutation in a DNA sequence by using a short synthetic oligonucleotide that hybridizes to the region to be mutated. With this technique, a single codon can be modified in a predetermined manner to cause the specific replacement of one amino acid by another in the protein gene product. Based on a knowledge of the relationship between the protein's structure and function, amino acid substitutions can lead to a modified (engineered) protein that has increased stability, increased catalytic activity, or altered substrate specificity. Although potentially a very exciting development in biotechnology, the applications of this technique are restricted at present by our limited knowledge of the factors relating protein structure to function in many of the proteins of commercial interest. Indeed, the technique is mainly used in basic research into an understanding of the factors relating protein structure and function.

Size-exclusion chromatography: *See* Gel filtration.

Sizing: The application of adhesive starch to fabrics to increase strength during weaving.

Slime layer: An "ill-defined" layer of polysaccharide exterior to the cell wall in some bacteria. *See also* Capsule, Glycocalyx.

Slug flow: A type of two-phase flow, particularly in gas–fluid systems, in which the gas forms large bubbles whose dimensions are similar to the cross-section of the fluid flow. This process occurs in flow through tubes, where the gas segments the fluid into discrete volumes (slugs) as in some forms of automatic analyzer equipment and gas-lift devices.

Snail gut enzyme: A commercial preparation of snail digestive juice used to degrade cell walls. Used in particular to prepare protoplasts, and sold as helicase, gluculase, or sulfatase.

Sodium azide (NaN_3): Often used as a bacteriostatic agent (at ≈0.02%) in buffers and solutions that are stored for any length of time and in buffers used in chromatographic columns, where bacterial contamination can cause clogging. Not to be used in solutions containing

horseradish peroxidase, as this enzyme is inhibited by sodium azide. Its bacteriostatic effect is caused by interference with the electron-transport chain.

Sodium dodecyl sulfate (SDS): $CH_3(CH_2)_{10}CH_2OSO_3Na$. An anionic detergent used to denature and solubilize proteins. Also known as sodium lauryl sulfate.

Sodium lauryl sulfate: *See* Sodium dodecyl sulfate.

Solid substrate fermentation: A process in which an organism is allowed to grow on a solid substrate (e.g., the Koji process). The solid is extracted to recover the desired microbial product after the optimum time for growth and production has been reached. Growth may take place in shallow trays or in large heaps, which may be turned either by hand or mechanically in rotating drums or in tanks with blown air and mechanical stirring.

Somaclonal variation: All types of variation that occur in plants regenerated from culture cells or tissues. *See also* Somatic variants.

Somatic: Referring to the vegetative (nonsexual) stages of a eukaryotic life cycle.

Somatic cell: Any eukaryotic cell other than a germ cell (egg or sperm in mammals, ovule or pollen in plants).

Somatic embryogenesis: *See* Embryogenesis.

Somatic hybridization: The fusing of two protoplasts or cells with different genotypes to produce hybrids that contain various mixtures of nuclear and cytoplasmic genomes.

Somatic variants: Plant-cell clones that differ from the parent cell. Although plants derived by vegetative means (clones) are usually like the parent plant, not all clones are genetically identical (*see* Clone). Clones that differ significantly from the parent are called somatic variants or sports, and are said to show somaclonal variation. Occasionally sports become established as important new varieties (e.g., the nectarine).

Somatotropin: *See* Human growth hormone.

Sonication: The use of ultrasonic energy to disrupt cells. The application of ultrasonics to a liquid causes areas of compression and rarefaction to occur. Cavities form in the areas of rarefaction, but rapidly collapse as the area changes to one of compression. Bubbles produced in the cavities are therefore compressed to several thousand atmospheres, and on their collapse shock waves are formed. These shock waves are thought to be responsible for cell damage. Generally only used for laboratory-scale work.

Southern blotting (Southern transfer): A method for transferring separated DNA fragments (e.g., a restriction enzyme digest) from an agarose gel to a solid support such as a nitrocellulose or nylon membrane. The method is named after E. M. Southern, who developed the technique. The DNA is first denatured in the gel by soaking the gel in sodium hydroxide. Transfer of the denatured DNA from gel to membrane is achieved by placing first the membrane and then a pad of adsorbent material on the gel. Buffer is allowed to soak through the gel, carrying the DNA from the gel to the membrane, where the DNA binds. The membrane therefore contains a replica of the DNA bands separated in the gel. The membrane can then be washed in a solution of an appropriate radiolabeled DNA or RNA probe, which binds to the DNA fragment of interest by complementary base-pairing. This binding can be detected by autoradiography.

Spacer arm: When an affinity adsorbent is constructed for affinity chromatography, it is often necessary for ligands to be held at some distance from the matrix. This distance avoids problems of steric hindrance between the ligate and matrix that would otherwise prevent correct binding. The ligand is therefore linked to the matrix via a spacer arm, usually a short alkyl chain 4–12 carbon units long.

Spacer groups (affinity chromatography): Chains of atoms, often carbon, that are chemically bonded to a stationary phase to provide the basis for derivatization to form the modified phases necessary for affinity chromatography. The chain length has an important bearing on the selectivity that may be obtained.

Sparger: A device for introducing air or oxygen into a reactor by way of an orifice that generates bubbles. The size of the bubbles and the velocity at which they rise in the fermentor determine the rate of oxygen transfer. *See also* Bubble column fermentor.

Specific ion electrode: *See* Ion-selective electrode.

Specific optical rotation: A measure of the rotation of the plane of polarization of plane-polarized light by an optically active substance. It is defined as:

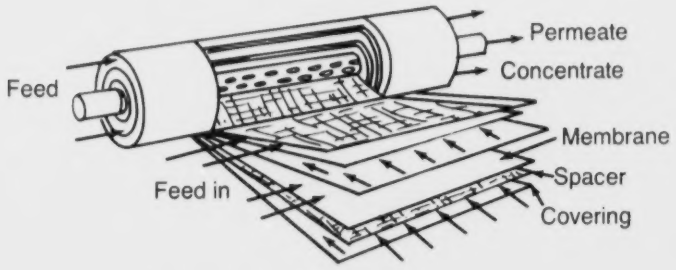
$$[\alpha]_{\lambda}^{T} = \frac{\alpha V}{lm}$$

where α is observed rotation, V is volume of sample, l is path length, and m is mass of solute or sample if it is a pure liquid. As the value of the rotation is dependent on wavelength of the radiation, λ, and temperature, T, these must be specified and are normally the sodium D line and 20 or 25 °C, respectively.

Specific viscosity: The difference between the viscosity of a solution or suspension and that of the solvent or continuous phase in which the species is dissolved or suspended, all measured at the same temperature.

Spheroplast: A bacterial or yeast cell that has been largely, but not entirely, freed of its cell wall, usually by enzymatic digestion, and that retains an intact cytoplasmic membrane.

Spirally wound module: A configuration for a membrane in which a sandwich of membrane(s) and spacers is wound into a spiral. The module produces a high surface area (800–1000 area-to-volume ratio) with both low investment and low operating costs. However, the module suffers from poor control of fouling and concentration or polarization effects. The module is used for both reverse osmosis and ultrafiltration where low fouling is expected.



Splenocytes: Lymphocytes isolated from the spleen.

Spontaneous mutation: *See* Mutation.

Sport: Any organism (or cell) with unusual characteristics produced by natural mutation. A mutant. *See also* Somatic variants.

Spray column: The simplest type of column contactor, in which one phase is introduced as a spray via a distributor to pass through the continuous phase in an unhindered pattern. An inefficient type of contactor, only used for the most favorable of processes.

Spray drying: A method for the large-scale recovery of dry solids from a concentrated aqueous solution or suspension. The solute or suspension is atomized in a drying chamber, into which a stream of heated air is introduced. The moisture evaporates into the air stream and the dried powder is collected. Reduced pressure is also sometimes applied to increase the rate of solvent evaporation.

Stacked-plate reactor: A reactor designed for the large-scale growth of mammalian cells. Circular glass or stainless steel plates are fitted vertically ~5 mm apart on a central shaft. The shaft is immersed in growth medium and can be stationary, with an airlift pump for mixing, or can revolve on a vertical or horizontal axis. The large surface area provided by the plates is ideal for the growth of anchorage-dependent cells. A 200-dm^3 reactor can give a surface area of 2×10^5 cm^2.

Stage (theoretical): *See* Plate (theoretical).

Standard oxidation–reduction potential: E^o is the potential of a redox couple when the activity of the oxidized form is equal to the activity of the reduced form of the species. Thus, from the Nernst equation:

$$E = E^o + \frac{RT}{nF} \ln \frac{a_{ox}}{a_{red}}$$

When $a_{ox} = a_{red}$, then $E = E^o$. E is the observed electrical potential, E^o is the standard potential, R is the gas constant, T is the absolute temperature, n is the number of electrons involved in the redox couple, F is the Faraday, and a is the activity of the species involved.

Starch: One of the major nutritional storage molecules in plants. It has two forms. One form, amylose, is unbranched and consists of glucose molecules in α-1,4 linkages. The other form, amylopectin, consists of chains of glucose α-1,4 linked with one α-1,6 linkage every 30 α-1,4 linkages. The main sources of industrial starch are maize, wheat, and potato. The hydrolysis of these starches on an industrial scale is achieved enzymatically. Following liquefaction (i.e., dispers-

ing and rupturing of the starch granules into aqueous solution by heating in the presence of a thermostable α-amylase), the starch is progressively hydrolyzed to dextrose (glucose) by the use of enzymes such as α-amylase (from *Bacillus subtilis*), amyloglucosidase (from *Aspergillus niger* or *A. oryzae*), and pullulanase to give a solution with a high (≈96) dextrose equivalent. This stage after liquefaction is known as saccharification. The glucose syrup product can be further processed to produce high-fructose syrups.

Starter culture: A term normally restricted to describing microbial inocula used to deliberately inoculate milk for the preparation of a range of milk products, such as butter, cheeses, and yogurt. The cultures, which may be bacterial or fungal strains and are used as pure or mixed cultures, have been selected for their ability to (1) produce lactic acid for curd production and a low pH value to prevent spoilage; (2) produce metabolites that give desirable flavors; or (3) produce enzymes that mature the dairy product.

Starter rotation: In cheese making, several cultures with susceptibility to different bacteriophage strains are used in rotation as inocula. This rotation reduces the likelihood that a particular bacteriophage will become established in a cheese-manufacturing plant and halt production.

Start-up: A term applied to the commencement of a process when the process conditions may vary from those found for continuous running.

Static maintenance reactor: A reactor design for the growth of mammalian cells. Some mammalian cells secrete products maximally when in an active growth phase, and others produce better when quiescent. The reactor is designed for the latter type of cells.

Stationary phase: The point at which growth ceases in a microbial culture. As log phase proceeds in a microbial culture, toxic byproducts tend to accumulate and the substrate (nutrient) becomes increasingly depleted until exhausted. Growth of the microorganism therefore slows down (*deceleration phase*) and finally ceases, at which point the culture is said to have reached the *stationary phase*. After a further period of time, the culture enters the *death phase*, and the number of viable cells declines.

Staverman reflection coefficient: *See* Darcy law.

Stem cells: Proliferating cells (eukaryotic) that can both maintain their own numbers by self-renewal divisions and give rise to differentiated progeny.

Stereoisomers: Forms of a chemical compound (isomers) that vary from one another in the spatial orientation of the atoms in the molecule. Various types of stereoisomer can be distinguished, such as optical isomers (stereoisomers that give rise to optical activity) and geometrical isomers (which depend on the nature of the groupings and spatial configurations and are termed *cis* and *trans*, *syn* and *anti*, *mer* and *fac*, etc).

Sterilization criterion: *See* Del factor.

Sticky ends: The ends of a double-stranded DNA molecule in which there are single-stranded extensions of nucleotides. *See also* Restriction endonucleases.

Stirred-tank reactor: A type of fermentor in which agitation is provided by a mechanically rotated stirrer or turbine.

Stoichiometry: In a chemical system the stoichiometry of the reactants is defined as the relative number of atoms or molecules taking part in a chemical reaction. In a biological system, because of its more complex nature and the uncertainty of the chemical composition of the components, a mass-based rather than a mole-based approach is used. This mass balance can be related to a number of parameters, such as total mass, carbon content, and chemical oxygen demand.

Stokes law: An equation that relates the velocity of a particle in a fluid to the viscosity of the fluid and the size of the particle. It is used as a basis for the falling-sphere viscometer, and also in the Stokes law tube as a means of removing particulate matter from a fluid stream prior to sampling in on-line analysis. Stokes law may be represented by

$$D = 6\pi\eta rV$$

where D is the drag on a sphere of radius r, falling at velocity V, in a fluid of viscosity η.

Strain gauge: A device for monitoring the extension or compression of an elastic material. An electrical resistance strain gauge is normally

a grid of metal foil, usually constantin alloy, deposited on a thin sheet of plastic material. Gauges are generally used with resistances of the order of 50–500 Ω. Strain gauges are used in load cells to monitor weight and also in fermentor agitator shafts to measure the power uptake.

Streamline flow: *See* Laminar flow.

Streptavidin: A protein from *Streptomyces avidinii* that has the same biotin-binding properties as avidin. Unlike avidin, it is not a glycoprotein and thus is said to cause less nonspecific binding.

Streptomyces: A genus of the actinomycetes that produces branching mycelia and aerial hyphae bearing chains of spores. They are common in the soil and are involved in the breakdown of a variety of organic compounds. Streptomycetes produce over 60% of the known antibiotics, including streptomycin and the tetracyclines. A number of *Streptomyces* species are being used in genetic studies, and over 100 genetic markers have been identified in *S. coelicolor*.

Stuffer fragment: *See* λ Replacement vector.

Subculture: A culture obtained by the subdivision of a culture and the transfer of one or more of these subdivisions into fresh culture media.

Submerged culture: Culture conditions in which the fermentation broth is agitated at sufficient rate to ensure equal distribution of the organisms throughout the medium and to ensure that concentration gradients of nutrients or oxygen do not build up and lead to local variations in growth conditions.

Subtilisin Carlsberg: A serine protease produced from *Bacillus licheniformis*. The enzyme is used extensively in enzyme washing powders; over 500 tons of pure enzyme is produced annually.

Sulfydryl (thiol) proteases: One of the four classifications used for proteases, based on the mechanistic action at the active site. Sulfydryl proteases have a functional thiol (–SH) group at their active site. Many of them, such as papain, bromelain, and ficin are isolated from plant sources.

Supercoiled plasmid: *See* Covalently closed circular DNA.

Supercritical extraction: The extraction of a substance using a supercritical fluid (e.g., carbon dioxide) as the solvent. The process takes place under a pressure greater than atmospheric, but has the advantage that release of this pressure causes rapid volatilization of the fluid that leaves the extracted material normally uncontaminated by solvent residues. This advantage, together with the relatively low temperatures involved during extraction, makes the process particularly suitable for foodstuffs and flavors.

Supercritical fluid chromatography: A chromatographic system that uses a supercritical fluid as a mobile phase with either a capillary gas chromatograph or packed-column HPLC equipment. A number of supercritical fluids can be used (e.g., ammonia, carbon dioxide, nitrous oxide), and their solvent properties can be modified by varying the pressure or by the addition of small amounts of polar liquids. The whole system operates at higher-than-atmospheric pressure because of the need to retain the fluid in its liquid state. The advantages include rapid separations with clean products uncontaminated by solvents. On release of pressure, these mobile phases rapidly evaporate, and thus facilitate the linking of the chromatograph to other analytical equipment.

Superinfection: A term used to describe the infection by a virus of a host previously infected by another virus. Not to be confused with *double infection,* in which two viruses invade simultaneously.

Surface activity: A term used to describe the variation of the surface tension of a liquid by the presence of a solute. As a result of the tendency of the free energy of a surface to decrease, the concentration of a solute on the surface may differ from that in the bulk phase. The component with the lower surface tension will tend to congregate at the surface, because in this way the surface energy is reduced. Thus if a given solute lowers the tension at a particular interface, then there will be a greater concentration of the solute in the interface than in the bulk phase (i.e., the solute will concentrate at the interface). Such solutes are said to display surface activity. *See also* Surfactants, Antifoam agents.

Surface fermentation: The growth of an organism on the surface of a static fermentation liquor, where the microorganism grows as a raft floating on the surface of the culture and the required product is collected from the aqueous medium.

Surfactants: A general term given to surface-active compounds (i.e., compounds with low surface tension that tend to congregate at a liquid–liquid interface). These compounds generally contain both hydrophilic (polar) and hydrophobic (nonpolar) groupings; they may carry an overall positive (cationic), negative (anionic), or neutral (nonionic) charge. They may be used as a means of dispersing oils in aqueous systems, as compounds for the transfer of charged compounds from an aqueous to organic phase (as in ion partition extraction), or to increase the gas–liquid interfacial area in a fermentor. In a fermentor, in addition to increasing the interfacial area, the presence of surfactant molecules at the interface may increase the mass-transfer resistance and reduce the mobility of the interface. However, the increase of interfacial area generally outweighs the other effects. Therefore the oxygen-transfer coefficient normally increases with increasing concentrations of surfactants at low overall concentrations.

Suspension culture: The growth of cells in submerged liquid culture.

: **(1) Plant cells**: Suspension cultures are usually initiated by transferring established callus tissue from a semisolid medium to a liquid medium. The liquid medium is then agitated and gives rise to a heterogeneous population of cells comprising a mixture of free-floating single cells and cell aggregates. Unlike mammalian cells, plant cells are not attachment-dependent. Single-cell suspensions from suspension culture can be plated out in semisolid media (in a manner very much like that used routinely in microbiology). Cell colonies that grow up (calliclones) can be transferred to new Petri dishes and grown on to form a callus. These callus cultures can then be induced (organogenesis or embryogenesis) to generate complete plants. *See also* Paper raft nurse technique.

: **(2) Animal cells**: Suspension culture is the preferred method for scaling up mammalian cell cultures. However, only hemopoietic and transformed cells grow naturally in suspension culture, because most other mammalian cells show anchorage dependence. Fortunately, a number of anchorage-dependent cells can be selected or adapted to grow in suspension culture, although a few will not survive in suspension at all. Because of the fragile nature of mammalian cells, they are best grown under conditions of minimum shear stress (e.g., in airlift fermentors). The encapsulation of cells in gelatin, alginate, agarose, etc., has also been used to protect cells from mechanical stress in other large-scale culture equipment (e.g., stirred fermentors). *See also* Microcarrier.

Svedberg unit (sedimentation): A unit of sedimentation equal to a sedimentation coefficient of 1×10^{-13} s.

Sweet sorghum: A tall grass with high sucrose content in the stems. It is widely grown for cattle forage, but has been used for ethanol production by fermentation.

Symbiosis: An association of dissimilar organisms to their mutual advantage, such as the association of nitrogen-fixing bacteria with leguminous plants (peas, beans, etc.). The bacteria inhabit nodules on the plant roots and synthesize nitrogenous compounds from nitrogen in the air. These nitrogenous compounds become available to the plant for metabolism. The bacteria obtain carbohydrates and other food substances from the plant.

Synergism: A phenomenon by which the additive properties of two components are greater than the sum of the effects of the two components taken separately. *Compare with* Antagonism.

Synergist: A compound that by itself has little activity, but when combined with another compound enhances the activity of the latter.

Syntrophy: Nutritional interdependence of two organisms.

Tailing: **In chromatography**: A term used to denote the asymmetry of a chromatographic peak, as shown by an elongation of the tailing edge.

: **In hydrometallurgy**: The solid residues remaining after processing that are normally deposited in heaps. Tailing heaps may be reworked for the metal resources they contain, especially with the aid of microbial leaching.

Takadiastase: *See* Koji.

Tangential-flow filtration: *See* Crossflow filtration.

Taxonomy: The classification of organisms into groups based on similarities of structure, origin, etc.

T-DNA: *See Agrobacterium tumefaciens.*

T4-DNA ligase: *See* DNA ligase.

T4-DNA polymerase: A DNA polymerase, isolated from bacteriophage T4, that also has a 5′ to 3′ exonuclease activity.

Temperature-sensitive (ts) mutation: A mutation in a gene that results in a gene product that is only functional within a certain tem-

perature range. For example, many laboratories use λ phage with a temperature-sensitive mutation in the gene *cI*, which is one of the genes responsible for maintaining the phage in the integrated state. At 30 °C, the gene is functional and lysogeny occurs, but at 42 °C the gene product is inactive and lysogeny cannot occur. Cultures are therefore grown at 37 °C and then induced to produce extracellular phages by transferring to 42 °C.

Template: Any polynucleotide that acts as a substrate for the synthesis of a complementary nucleic acid strand (e.g., mRNA acts as a template for reverse transcriptase in the synthesis of cDNA).

Terminal transferase (terminal deoxynucleotidyl transferase): An enzyme isolated from calf thymus tissue that adds one or more deoxynucleotides to the 3'-terminus of a DNA molecule. The enzyme is used for homopolymer tailing of DNA molecules for later cloning.

Thaumatin: An intensely sweet-tasting, nonnutritive protein from the fruit of the African plant *Thaumatococcus danielli*. Aqueous solutions of thaumatin have an intense sweetness about 1600 times that of a 10% sucrose solution. It is sold under the trade name "Talin" and is used in the food and drink industry.

Theoretical plate: *See* Plate (theoretical).

Theoretical stage: *See* Plate (theoretical).

Thermistor: A device used to monitor temperature, with which changes in temperature are detected by a change of resistance within a semiconductor.

Thermistor-based sensors: Sensors that use a thermistor device to monitor small temperature changes generated in biochemical reactions. Temperature changes in the range 0.01–0.001 °C are usually recorded.

Thickening: The process of concentrating suspended solids and separating them from the contained liquor, generally carried out under gravity.

Thimerosal: Sodium ethylmercurithiosalicylate. Often used as an antimicrobial agent in buffers, solutions, etc., that are stored for any length of time and in buffers used in chromatographic columns in

which bacterial contamination can cause clogging or degradation of column materials.

Thiobacillus ferrooxidans: *See* Microbial leaching.

Thiol proteases: One of the four possible classifications of proteases. Thiol proteases have a thiol (–SH) group at the active site that is essential for activity. *See also* Papain, Ficin, Bromelain.

Thixotrophy: A time-dependent reversible behavior of a fluid under an applied shear stress, such that on application of a shearing force the fluid becomes less viscous. When the shear force is removed, the viscosity returns to its original value.

Thylakoids: Membranous structures, shaped like flattened sacs, found in chloroplasts. A pile of these sacs is a granum. The thylakoid membranes contain the chlorophyll molecules and other components of the energy-transducing machinery necessary for photosynthesis.

Ti plasmid: *See Agrobacterium tumefaciens.*

Tissue culture: The process whereby small pieces of living tissue (explants) are isolated from an organism and grown aseptically in a defined or semidefined nutrient medium. Originally the term was used to describe the culture of whole fragments of explanted tissue. Currently the term covers both *organ culture* (in which a piece of tissue or embryonic organ explant is grown and retains tissue architecture, cell interaction, and histological–biochemical differentiation) and *cell culture* (in which explant tissue is dispersed enzymatically or mechanically, and propagated as a cell suspension or attached monolayer).

Tissue plasminogen activator (t-PA or TPA): A mammalian enzyme that converts plasminogen into its active form, plasmin. Plasmin then dissolves fibrin, which is the major component of blood clots. The enzyme has proved to be particularly successful in the clinic for dissolving blood clots in heart-attack victims. It is presently being produced by recombinant DNA technology by a number of biotechnology companies. t-PA's promise lies in the specificity with which it dissolves blood clots but does not cause widespread bleeding in the patient. Currently approved plasminogen activators such as streptokinase and urokinase do not bind to fibrin, so they activate plasminogen throughout the blood stream. This activation leads to systemic degradation of blood proteins such as fibrinogen, which causes internal bleeding as well as blood clot dissolution.

Toprina: *See* Single-cell protein.

Toroidal chromatography: *See* Countercurrent chromatography.

Torque: A force that results from the rate of increase of the moment of momentum for rotating bodies, the magnitude of which is the product of the momentum and the normal distance of the point of application from the axis of the rotating body.

Tortuosity: A term used to describe the nature of the pore structure within a solid, which takes account of the deviation of these pores from a straight-line configuration. A system that follows a straight line is given a tortuosity of unity, so that the higher the value, the greater is the path length followed by the pore channel.

Torula yeast: A contaminant in some milk products that is responsible for unwanted alcohol fermentation.

Total dissolved solids (TDS): The total mass of material in a filtered solution after drying at 105 °C. Units are milligrams per cubic decimeter or parts per million.

Total filterable residue: *See* Total dissolved solids.

Total nonfilterable residue: *See* Total suspended solids.

Total organic carbon (TOC): A measure of the carbon (organic) content of a sample, especially in the case of water, where it may be used as a measure of pollution. The technique used for its determination involves pyrolysis of the sample in oxygen, followed by analysis of the evolved carbon dioxide.

Total oxygen demand: The amount of oxygen consumed in the combustion of organic compounds in a sample at 900 °C.

Total suspended solids (total nonfilterable residue): The total dried solid material retained by a standard fiberglas filter following filtration of a well-mixed sample. Alternatively, the dried solid material separated by centrifugation. These residual solids are dried at 103–105 °C, weighed, and recorded as milligrams per cubic decimeter or parts per million.

Totipotent: Descriptive of a cell that is able to generate the complete and differentiated organism from which it was derived. For example,

callus cells can be induced to form either embryos (embryogenesis) or roots and shoots (organogenesis), which then develop into full plants.

Tower bioreactor: An elongated tubular vessel for carrying out fermentations. There is no mechanical agitation of the culture. Air is introduced at the bottom of the tower, and mixing is produced by the rising bubbles. This method produces very little shear effect on the organisms.

***trans* Configuration**: A term used to describe stereoisomers in which similar groups are on opposite sides of a double bond. *Compare with cis* Isomers.

Transducer: A device that converts a measurable parameter into a signal, commonly an electrical signal whose magnitude is related to the magnitude of the original parameter. *See also* Biosensor.

Transduction: The transfer of genetic material from one cell to another by means of a viral vector, and the subsequent incorporation of this genetic material (by recombination) into the genome of the recipient cell.

Transfection: **(1)**: The introduction of DNA into cultured cells.

: **(2)**: The introduction of purified phage DNA molecules into a bacterial cell.

Transfer genes (*tra*): *See* Self-transmissible plasmids.

Transformant: *See* Transformation.

Transformation: **(1)**: Any alteration in the apparent growth properties, morphology, or behavior of a cell in culture.

: **(2)**: The acquisition of new genes in a cell after the incorporation of nucleic acid (usually double-stranded DNA) into the cell (e.g., the introduction of a plasmid into a bacterial cell). The bacterial cell is then said to have been transformed and is referred to as a *transformant*.

Transformation efficiency: In a transformation experiment, the number of transformants produced per microgram of cloning-mixture DNA.

Transformation frequency: A measure of the proportion of cells in a population that are transformed in a given experiment.

Transformation processes: The use of microorganisms to catalyze the conversion of a compound into a structurally similar (and normally more commercially useful) compound. For example, the production of vinegar (the conversion of ethanol into acetic acid) is a well-established transformation process.

Transgenic animal: An animal whose genetic composition has been altered to include selected genes from other animals or species by methods other than those used in traditional animal breeding.

Transmission (%*T*): A measure of the amount of radiation transmitted by a sample, used in particular for IR spectrophotometry, and defined by

$$\%T = \frac{100\ I}{I_o}$$

where I is the transmitted radiation intensity and I_o is the incident radiation intensity. Related to absorbance by

$$A = 2 - \log \frac{1}{T}$$

Transmittance: In spectrophotometry, the relative amount of radiation transmitted by a sample:

$$T = \frac{I}{I_o}$$

where I is the transmitted intensity of radiation, I_o is the incident radiation intensity, and T is the transmittance.

Tray column: *See* Plate column.

Triazine dyes: *See* Dye–ligand chromatography.

Trickling filter: *See* Percolating filters.

Trisacryl: Synthetic gels formed by the polymerization of *N*-acryloyl-2-amino-2-hydroxymethyl-1,3-propanediol. The resulting polymer has three hydroxymethyl groups and one alkylamide group per re-

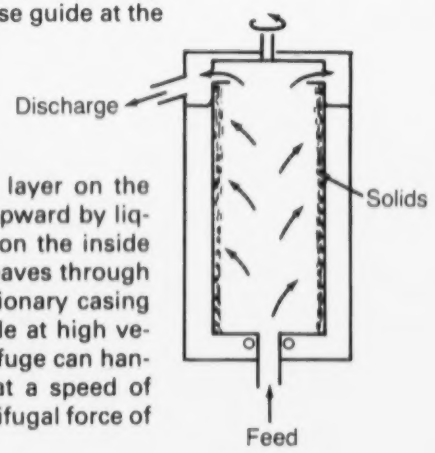
peating unit. It can be used as a gel-filtration medium, or as an ion-exchange and affinity chromatography support.

Triton X-100 (isooctylphenoxypolyethoxyethanol): A nonionic surfactant used to dissolve cytoplasmic membranes without causing the denaturing of proteins (Rohm and Haas trademark).

Trophophase: The log or exponential phase of a culture, during which the sole products of metabolism are either essential to growth (such as amino acids, nucleotides, proteins, lipids, and carbohydrates) or are the byproducts of energy-yielding metabolism (such as ethanol, acetone, and butanol). The metabolites produced during the trophophase are referred to as primary metabolites. The term trophophase is therefore descriptive of the behavior of microbial cells based on their metabolism, whereas the equivalent terms "log" or "exponential phase" describe the kinetic behavior of the cells.

Trypsinization: The generation of primary-culture cells by disaggregating tissue by the use of a trypsin solution.

Tubular bowl centrifuge: A type of centrifuge in which the bowl is suspended from the top and hangs free, with only a loose guide at the bottom. Feed enters at the bottom through a stationary nozzle, under sufficient pressure to jet it upward into the bowl. The fluid is accelerated toward the bowl and forms a layer on the inside wall. Solids are drawn upward by liquid flow, and particles collect on the inside walls of the bowl. The liquid leaves through the top of the bowl into a stationary casing and exits via a discharge nozzle at high velocity. A 10-cm-diameter centrifuge can handle from 5 to 45 $dm^3\ min^{-1}$ at a speed of 15,000 rpm, to generate a centrifugal force of 14,000 *g*.



Tubular membrane module: A configuration of membranes used in crossflow, micro-, and ultrafiltration processes with high solids content. The membranes are formed into tubes 1–2 cm in diameter supported by rigid porous shells. This design results in a low membrane area to tube length ratio (i.e., 20–30 m^{-1}) and high investment and

operating costs. However, the system does allow control of membrane fouling and concentration polarization.

Turbidity: Turbidity is a measure of the amount of light scattered by the presence of microscopic suspended matter in a fluid. It may be determined by a turbidimeter, in which a collimated light beam is passed through the sample and the turbidity is measured by the apparent increase in the absorbance. *See also* Nephelometry.

Turbidostat: A continuous-culture vessel in which fresh medium flows in response to an increase in turbidity of the culture. *See also* Continuous culture.

Turbulent flow: Fluid flow in which fluid particle motion at any point varies rapidly in direction and magnitude. Characteristic of fluid motion at high levels of mixing and high Reynolds number. *See also* Laminar flow, Plug flow, Reynolds number.

Turnover number: In enzymology, the number of substrate molecules processed by one enzyme molecule per second. Typically, enzymes have turnover numbers of the order of 10^4, but some have values as high as 10^8.

Two-phase aqueous partitioning: The distribution or partitioning of a substance between two partially miscible phases largely composed of water. A typical phase system is polyethylene glycol–dextran–water, which separates into two phases, one largely polyethylene glycol–water and the other largely dextran–water. These systems are used widely for the partitioning of cells, as well as proteins and other substances. They have the advantage that, because of the high water content of the phases, biological materials do not become denatured. However, they have the disadvantages of (1) long phase-separation times, as a result of little difference in density between the phases and very low interfacial tensions; (2) relatively high viscosities; and (3) high cost of scale-up, as the partial miscibility of the components means that a significant percentage of them cannot be recycled.

Two-phase reactions: Enzyme reactions carried out in the presence of a second water-miscible phase, such as an organic solvent. This procedure allows high concentrations of water-insoluble substrate to be maintained. However, enzyme denaturation by the organic solvent can be a problem with this method. Alternatively, the second phase can be a water-immiscible solvent. The reaction is carried out in a stirred reactor that maintains a fine emulsion, with the enzyme pres-

ent and stable in the aqueous phase but in close association with the substrate in the organic phase.

Tylosin: An antibiotic produced commercially by strains of *Streptomyces fradiae*. It is used exclusively for animal nutrition (for improved feed efficiency and growth promotion) and in veterinary medicine. Tylosin contains a 16-membered lactam ring with three sugars (mycarose, mycaminose, and mycinose) attached.

Ultracentrifuge: A high-speed centrifuge used for the separation and analysis of macromolecules (e.g., proteins, nucleic acids). The high *g* forces (up to 500,000 *g*) generated by the centrifuge cause sedimentation of the molecules according to their molecular weight, density, and shape. When a density gradient is generated within the supporting fluid, molecules may be separated into bands as their density matches that of the supporting fluid. *See also* Density gradient centrifugation.

Ultrafiltration: A membrane filtration process using an asymmetric microporous polymeric membrane with pore sizes of 1–50 nm, driven by a hydrostatic pressure of 200–1000 kPa. Separation of components from the mixture takes place by a sieving mechanism, with the open structure of the membrane on the feed side and the fine porous "skin" on the downstream side of the process. This arrangement allows the macromolecules to enter and be retained by the membrane. Thus they are separated, concentrated, and purified from smaller molecules, salts, etc., with molecular weights less than about 3000, which pass through the porous "skin".

Ultrafiltration reactor: A biochemical reactor, mainly used for carrying out enzyme-catalyzed depolymerization reactions, that incorporates an ultrafiltration membrane to separate low- and high-molecular-weight components.

Ultrasonics: A term used to denote frequencies of 20 kHz and above.

Ultraviolet radiation (applications): UV radiation occupies a wavelength range between visible and X-radiation, with the normal useful range between 200 and 400 nm. Because many organic molecules absorb in this range, UV spectroscopy can be used for qualitative and quantitative analysis (e.g., scanning of gels for the detection of DNA). Because of the increased energy involved in UV radiation, it can also induce bond fissión in photochemical reactions and cause the destruction or modification of microorganisms, as in mutation programs and UV sterilization.

Undefined medium: A microbial growth medium in which not all the components have been identified. Also known as a complex medium.

Upflow: The opposite of downflow as a regime for the operation of columns in, for example, chromatography or extraction processes. The passage of a mobile phase against gravity.

Upstream: In a process flowsheet, upstream processes come before the main reactor (e.g., fermentor). Converse of downstream.

***Vaccinia* virus**: A large double-stranded DNA virus that has been used extensively to eradicate smallpox. Inoculation with *Vaccinia*, which is harmless in humans, confers resistance to smallpox because of production of antibodies that cross-react to the smallpox virus. *Vaccinia* virus has also been developed as a cloning vector. Live recombinant viruses express foreign antigens on their surface, and can therefore be used as immunogens. For example, a *Vaccinia* recombinant containing the coding sequence for the rabies surface glycoprotein has been constructed. When injected into animals, this live hybrid virus protects the animals against later exposure to rabies. This protection stems from the production of antibodies directed against the rabies surface glycoprotein expressed on the surface of the *Vaccinia* virus. Other genes that have been expressed in *Vaccinia* recombinants include Hepatitis B virus surface antigen, *Herpes Simplex* virus glycoprotein D, Epstein–Barr virus glycoprotein, and influenza virus hemagglutinin.

Vacuum centrifuge: *See* Centrifugal concentrator.

Vacuum fermentation: The removal of volatile fermentation products during fermentation under vacuum so that the products distill at the normal fermentor operating temperature. A low concentration of products in the fermentor is maintained so that inhibition of the reaction is minimized. The process can also be operated with a bleed stream to remove nonvolatile byproducts.

Van Deemter equation (chromatography): An equation that relates the plate height (H) of a gas chromatographic column to the linear gas velocity (u) and has the form:

$$H = A + \frac{B}{u} + Cu$$

where A, B, and C are constants. The eddy diffusion term, A, describes the band broadening caused by variation of the gas velocity as a result of the porous structure of the column packing. The term B/u represents band broadening as a result of longitudinal diffusion of the solute molecules in the gas phase, and Cu is related to the mass-transfer resistance that inhibits the equilibration of solute molecules between the gas and stationary phases. The equation represents a hyperbola that produces an optimum gas velocity at which the height of the plate is a minimum.

Variation: *See* Somatic variants.

Vector (cloning vehicle): A DNA molecule, usually a small plasmid or bacteriophage DNA capable of self-replication in a host organism, and used to introduce a fragment of foreign DNA into a host cell. Commonly used vectors include plasmids, λ phage, SV40, and Ti plasmids from *Agrobacterium tumefaciens.*

Vegetative propagation (cloning): The asexual propagation of plants, either by detaching some part of the plant (e.g., a leaf cutting, shoot cutting) and growing the cutting in an appropriate medium such that a complete plant subsequently develops, or by the generation of whole plants from callus tissue culture or protoplasts.

Velocity gradient: A term denoting the rate of change of velocity with distance in a fluid; also termed shear rate.

Verticillium lecanii: A fungus, commercial preparations of which are now marketed for control of aphids in greenhouses and on crops grown under humid conditions.

Vesicular–arbuscular (VA) mycorrhiza: A form of endomycorrhiza arising when phycomycete fungi of the family *Endogonaceae* invade root cortical tissues and form a symbiotic association beneficial to the host. Most plants of agricultural importance have VA mycorrhiza. The agricultural importance of VA mycorrhiza lies in its ability to assist phosphate absorption by the plant from the surrounding soil. Because

phosphate ions are not very mobile in soil, phosphate depletion zones often form around roots when phosphate is in low supply. Mycorrhizal hyphae extend from the mycelium within the root to beyond the depletion zone and transfer phosphate directly to the host.

Vincristine: A plant alkaloid, isolated from *Catharanthus roseus* and used as an antitumor agent.

Virulence plasmids: Plasmids that are pathogenic to the host cell (e.g., Ti plasmids of *Agrobacterium tumefaciens* induce crown gall disease on dicotyledonous plants).

Viscoelasticity: The partial elastic recovery of a fluid upon the removal of a deforming shear stress.

Viscosity: One of the fundamental parameters of rheology; relates the shear stress (force applied) to the shear rate of a fluid, which may be time-dependent or time-independent. Many equations relate the two parameters, depending on the nature of the fluid (e.g., Newtonian, pseudoplastic, plastic, dilatant, thixotropic, rheopectic, or rheodestructive).

Vitis vinifera: Species of grape from which nearly all the world's wine is made.

Voidage: The proportion of a packed column or bed that is not occupied by solid material (e.g., that volume occupied by the fluid surrounding the solid particles).

Void volume (chromatography): A term used in chromatography to denote the elution volume of a substance that is not retarded in any way during the passage through the column. It is equal to the voidage of the column, and may be determined by injection of a substance that is not retained on the column under the conditions used.

Volumetric distribution coefficient (K_d): A parameter used in exclusion chromatography and gel chromatography to specify the fraction of the volume within the gel that is accessible to the solute. It is determined from elution data by:

$$K_d = \frac{V_e - V_o}{V_i}$$

where V_e is elution volume; V_o is void volume; and V_i is internal

volume. K_d can take values from zero, for solutes excluded completely from the gel, to unity, for solutes whose permeation equals that of the solvent. When values greater than unity are obtained, binding between the solute and the gel matrix has occurred.

Volumetric mass-transfer coefficient: *See* K_La.

Volumetric oxygen-transfer coefficient: *See* K_La.

Warburg apparatus: A manometric device used to follow changes in gas uptake or evolution in biological systems.

Water activity: A parameter that describes the fraction of free water in a solution. By definition, the water activity of pure water is unity. A low water activity of a solution corresponds to a high osmotic pressure of the solution. Microorganisms can grow only in media with a water activity level between 0.999 and 0.650. In general, a reduction in the water activity will strongly inhibit growth. Microorganisms that are able to grow at low water-activity levels are called osmotolerant.

Water-transport number: In dialysis, this is a measure of the ratio of the weight of water transported per unit weight of dissolved solute.

Western blotting: *See* Protein blotting.

Wheat-germ lysate: *See* Cell-free translation system.

Whey: The watery product remaining when the curd is separated from the remaining milk in cheese production. It contains high concentrations of lactose (≈50 g/L), as well as minerals, vitamins, and lactic acid. Disposing of waste whey, which is produced daily in considerable quantity, has been a problem for some time in the cheese

industry. The recent introduction of the use of lactase (isolated from *Aspergillus niger*) to convert whey into a sweeter solution of glucose and galactose, which is of use to the confectionary and baking industry, has had some success in overcoming this problem. Whey is also used as a substrate for the growth of *Penicillium cyclopium* to produce single-cell protein in the French "Heurtey" process.

Whirlpool separator: An alternative name for a hydrocyclone, used commonly for the separation of spent grain from brewing mashes. *See also* Hydrocyclone.

Wild type: The naturally occurring (nonmutated) form of an organism. Also used to refer to the nonmutated form of a specific gene in an organism.

Wiped-film evaporator: A modification of a rising- or falling-film evaporator, in which the walls of the heat exchanger are wiped by a rotating device (such as a metal strip or coil) to ensure that the concentrated material does not foul the heat exchanger and to minimize heat degradation of the substance.

Wort: The aqueous extract obtained after adding warm water to crushed malt (malted barley). In beer and lager manufacture, after separation of the wort and addition of hops, it is boiled, cooled, inoculated with brewers' yeast, and allowed to ferment.

Xanthan gum: A five-sugar repeat-unit polysaccharide with a molecular weight in the range 0.2–1.5 × 10^7, produced extracellularly by *Xanthomonas campestris* strains. The gum produces high viscosity at low concentrations and therefore has a wide range of industrial applications as an agent for viscosity control, in gelling and suspension, as a stabilizer, and in oil-recovery processes. In the food industry it is used to modify the texture of a wide range of foods.

Xenobiotic: A chemical compound not normally produced by living organisms; a synthetic compound. Organic compounds can be classified as biogenic (of natural origin) or anthropogenic (synthetic). Biogenic compounds are normally degradable by microorganisms, as are natural products produced on a large scale by synthetic routes. However, xenobiotic compounds, because of their unnatural structures, are degraded poorly (recalcitrant compounds) or not at all (persistent compounds) by microorganisms.

X-gal: A lactose analogue (5-bromo-4-chloro-3-indolyl-β-D-galactopyranoside) that is broken down by β-galactosidase to give a blue color. It is used, for example, to differentiate transformants containing the plasmid pUC8 (which synthesize β-galactosidase) and transformants containing plasmids (which have undergone insertional inactivation of the β-galactosidase gene).

X-Press: An apparatus used for rupturing microbial cells (e.g., yeast cells). A frozen paste of cells is disrupted by passage through a perforated disk, with an outlet temperature of ≈22 °C. Rupture of cells is caused by the shear forces exerted by the passage of the extruded paste through the small orifice; the shear is aided by ice-crystal formation in the frozen paste. *See also* Hughes press.

Xylan: A major component of plant hemicellulose. After cellulose, it is the most abundant renewable polysaccharide in nature. The main component of xylan is D-xylose, a pentose, but the structure of xylan is variable. It ranges from linear 1,4-β-linked polyxylose chains to highly branched heteropolysaccharides, which contain sugars other than xylose. Appreciable quantities of xylan are present in materials released from wood during pulping or pulp processing, but this is regarded as waste and is discarded. The development of enzyme processes that would convert xylan waste to fermentable sugars would be economically beneficial.

Yeast episomal plasmids (YEps): Any vector derived from the 2-μm circle plasmid of yeast (e.g., plasmid pJDB 219). *See also* Shuttle vector).

Yeast integrative plasmids (YIps): Bacterial plasmids that carry a yeast gene. They are unable to replicate within a yeast cell unless they are integrated into a chromosome. Integration occurs as a result of crossing-over between the yeast segment on the plasmid and the homologous gene on the chromosome.

Yeast replicative plasmids (YRps): Yeast plasmids that can multiply as independent plasmids in yeast because of the presence of a chromosomal DNA sequence containing an origin of replication. *See also* Autonomously replicating sequences.

Yeasts: Fungi that are usually unicellular for part of their life history, but may also form pseudomycelium or short lengths of true mycelium. The common method of vegetative reproduction of many yeasts is by budding. There are approximately 500 yeasts that belong to the Ascomycotina, Deuteromycotina, and Basidiomycotina. Yeasts are very important for baking, brewing, wines, spirits, single-cell protein, enzymes, and as a vitamin source.

YEps: *See* Yeast episomal plasmids.

YIps: *See* Yeast integrative plasmids.

YRps: *See* Yeast replicative plasmids.

Zanflo: A high-viscosity polysaccharide, comprising fucose, galactose, glucose, and uronic acid residues, produced from *Erwinia tahitica*. Used for carpet printing.

Zeatin: A naturally occurring cytokinin obtained from corn (maize) grains.

Zonal centrifuge: A type of centrifuge intended for the purification of viruses or the isolation of RNA, DNA, etc. The bowl is filled with a liquid that can establish a density gradient, and the feed is introduced into the bowl. The particles sediment into a band where the density equals that of the surrounding liquid. The bowl rotates in a vacuum at high speed, generating a maximum *g* number of 100,000 or over.

Zygomycotina: The division containing the fungi that have hyphae without cross walls and that reproduce sexually by the production of zygospores that result from the fusion of gametangia that may differ in size. These fungi normally reproduce asexually with the formation of sporangia containing sporangiaspores. Many genera in this group cause spoilage of a range of materials.

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